A TREATISE ON

MATERIA MEDICA,

(Including Therapeutics and Toxicology)

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Translated from the Fourth Enlarged Edition

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PREFACE.

The third edition of this work was published in 1877. It was in this edition that the work which had previously been edited alone by Dr. Nothnagel, received the aid of Dr. Rossbach. It was the latter who devised and executed the present mode of classification and to whom the care of the physiological action and chemical relations of the drugs was assigned, while Dr. Nothnagel assumed charge of the therapeutics, the toxicology and the preparation of the drugs. The authors in the preface to their third edition enter into the following explanations.

"Wherever chemistry has made known the essential active ingredient of a drug, this has received prominence, while drugs which were correlated but whose active principles were as yet unknown were treated of in the Appendix." "Modern chemical and botanical names were everywhere selected."

"The determination to abandon the old method of arranging the classification upon the basis of the physiological or therapeutical action of drugs was adopted, because of the widely different physiological and therapeutical effects which so many drugs have upon the different systems of the body and in varying diseased states."

"In our classification, which rests pre-eminently upon a chemical basis, we have sought to portray the present status of our scientific knowledge, even in its weak points. It will be demonstrated we hope that the chemical grouping of drugs is at the same time the best possible physiological classification; our insight into the physiological action of drugs has advanced sufficiently far to furnish us with guides to a narrower classification, in cases where our chemical knowledge is deficient; but in these cases our arrangement depends not upon the similarity of action in respect to a single organ, but upon the effects produced *upon all* the organs of the body." "In the *physiological consideration* of materia medica we started with *the idea, that the time* had arrived when the as yet separate

departments of drugs, poisons and food products should be united. It was simply in deference to the old custom that we retain the term "Materia Medica" upon the title page. Wine, Coffee, Tea, and Opium or Egg Albumen, Fats, and Carbohydrates are not worse remedies because they belong to our food products. We should also remember that frequently the required effect for the alleviation of some diseased states is consequent upon strong poisonous doses only, as is the case with the Caustics and Narcotics.

"We consider Materia Medica or Pharmacology as that portion of physiological science which treats of the reactions of the healthy and diseased organism to all chemically acting substances, and for this reason, in the physiological division, we include the effects of small dietetic and therapeutic as well as of large poisonous doses. This method alone can furnish the physician, in one work, with all that is worth knowing of every remedy, so that he can select what is useful or beneficial to mankind." In alluding to the therapeutical portion of their work the authors in the same preface say:

"We have not hesitated to give utterance to a belief in the uselessness of many well liked, and still frequently prescribed remedies, when they have been proved insufficient for the accomplishment of accepted indications, or can be replaced by better agents and means."

"In regard to the selection of the remedies we have not been able to adhere to the German Pharmacopœia, because the progress of science has far surpassed it; we have marked with a "star" all remedies not found in it. Further in reference to the maximum doses of the Pharmacopœia they correspond with our own, only in those cases where they proceed from the spirit of the decimal system, and that wherever this was not the case, we have made changes in accordance with the decimal system."

In the preface to the fourth edition July, 1880, from which the present was translated, we quote from the authors as follows:

"Our critical task to point out all uncertain drugs and indications has been adhered to, yet we could not, in spite of our personal inclination, pass over these, in the complete silence, which for various reasons might have been desired. We were deterred from this by the view that we were in a transition period and that the student and physician would frequently wish *to know why this or* that remedy no longer finds an *[illegible]tion.*"

In conclusion the translators beg to say that they feel certain that the clear classification of the remedies in this volume will materially help the student of experimental therapeutics, as well as any seeker after new remedial agents. That to the practitioner debarred by ignorance of the German language from previous acquaintance with the work it presents one of the best digests of our knowledge of remedies now extant.

Finally although many remedies or preparations may not be found in our own pharmacopœia, rules for their preparation are clearly given, thus facilitating and encouraging their use, wherever this may for any reason seem desirable.

H. N. Heineman.
H. W. Berg.

New York, 1883.

MATERIA MEDICA

AND

THERAPEUTICS.

CHAPTER I.

THE ALKALIES AND THE ALKALINE EARTHS.

Of the five alkaline metals, potassium, sodium, lithium, caesium and rubidium, only the hydroxides (which are the strongest bases and are termed alkalies) and salts of the first three are used in medicine. Of the metals of the alkaline earths only the strong basic oxides (the alkaline earths) and the salts of calcium and magnesium are used.

PHYSIOLOGICAL IMPORTANCE.

Some of the alkaline salts are normal and necessary ingredients of the animal body, most of the organs and fluids of which have an alkaline reaction. The sodium and potassium chlorides as well as the carbonates and phosphates of potassium, sodium and calcium, take a particularly prominent part in the performance of the animal functions; as will appear from the following consideration of the most important relations of these salts.

1st. It is exceedingly probable, that at least some of the albuminoid matters of the blood are held in solution by means of its alkaline reaction; for the albuminoid bodies found in the blood have an alkaline reaction due to the free alkali of the blood; again some solutions of albuminoids (globulin) can be made to precipitate the albuminoid matter, when carefully neutralized with acetic acid and diluted with water; further, the addition of some carbonate of sodium to albumen in solution raises the coagulation temperature, while the addition of

some other neutral alkaline salt diminishes it. Even if the importance of the alkalies for the solution of albumen has been shown to be problematical by Aronstein, still it remains good as far as paraglobulin is concerned, which is precipitated in increased amount, in proportion as its solutions are deprived of these salts by diffusion.

2nd. It has been particularly well shown by Liebig, that the alkaline reaction of the blood is of the first importance to the organic oxidation processes, that is to say to the production of heat and to decomposition; for it is only in the presence of a free alkali that many organic substances become capable of uniting with oxygen, and thus being burnt up, which, without an alkali would be an impossibility at the ordinary temperature of the body. In this way, alcohol in the presence of a free alkali is oxidized at the ordinary temperature; so also milk and grape sugar, which, with slight warmth, will even combine with the acid already in combination with metallic oxides. Under this condition even glycerine, ordinarily indifferent to ozone, will undergo rapid oxidation.

Many facts prove that this action of the alkalies takes place in the blood during life. The salts of malic, citric, tartaric and other vegetable acids, which we consume with fruit, are as thoroughly burnt up in our blood, as if they were acted upon by fire, and appear in the urine as carbonates. If however we introduce into the stomach these same organic acids free and not in combination with the alkaline bases, they reappear in the urine, for the most part unchanged and unconsumed. This is even the case with such easily oxidized acids as gallic and tartaric acids. Liebig accounts for this fact, by supposing that the neutral salts of the vegetable acids do not alter the alkaline reaction of the blood, while the free acids, by uniting with a portion of the alkali of the blood, diminish its alkalinity and deprive it of the power of oxidizing the whole of the acid which has been absorbed. Had the blood which has absorbed the gallic acid, for instance, remained strongly alkaline, then this acid would have been entirely destroyed; the presence of a free alkali and oxygen are incompatible with the existence of gallic acid.

3rd. The alkalies of the blood have not only the function of combining with the acids introduced with the food, but also with those produced in the tissues of the body as a result of the metamorphosis of other materials, as for example carbonic acid and phosphoric acid. We have then in the living body the great chemical antagonism between alkalies and acids

aiding, on the one hand, in the introduction of substances into the body (absorption of the acid chyle into the alkaline blood), and on the other, in the removal with the secretions of the final products of disintegration (carbonic acid, etc.) out of the cells, and through the whole economy. The interchange of substances in the body is only possible, because of the counteraction of the alkali of the blood and the acid of the living cell.

4th. Inasmuch as fats are saponified by ozone only in the presence of a free alkali, Gorup-Besanez believes himself warranted in ascribing to the free alkali present in the living blood an important function in the oxidation of the fats.

5th. The salts of the alkalies and the alkaline earths are of equal importance to the life of the organized cell. The most important organic molecule, the white of an egg, is found in the organism combined with salts, namely lime phosphate. There is no cell without a mineral ingredient, and some cells, as the bone corpuscle, fulfill their function of being the support of the body, only by means of the large amount of salt which they contain. We can distinguish two classes of salts, one of which (lime and magnesium phosphate, and lime carbonate) is important on account of the physical quality of giving firmness to the tissues ; the other, because of chemical characteristics (sodium and potassium chloride and alkaline phosphates).

Taking these facts into consideration it is not surprising that a constant supply of these salts is absolutely necessary to life ; that, indeed, the albuminoid bodies, without these salts, cannot support life, and that a want of salts in the food would soon result in death. Forster, in a series of valuable investigations, has arrived at the following conclusions concerning the importance of the salts for nutrition.

1st. Beginning with the healthy animal body in which the different constituents of the tissues are normally proportioned, it is necessary that certain salts be supplied, in order that the body may be maintained in this condition. Should this supply fall below a certain limit, or be entirely withdrawn, then the salts of the body diminish, and the body dies even though the other forms of food, such as albuminoids, fat and starch are given in sufficient quantity.

2nd. In the adult animal, deprived entirely of the mineral ingredients of the food, the processes of metamorphosis, growth and decay *continue in the* body, until the death of the animal *in the same manner* as when the animal was fed upon a diet *containing a small* amount of the inorganic ingredients, in ad-

dition to the other necessary ingredients of the food. Soon disturbances in the functions of the organs occur, which finally result in the destruction of the organism. These act, partly, by preventing the modifications which the food undergoes in order that it may be fitted for absorption, and thus replace the waste of the tissues, (such disturbances are for instance anorexia, dyspepsia, vomiting of all food, etc.), and partly by interfering with processes of great importance to life, such as would be caused by a functional weakness of the brain, spinal cord, motor or sensory paresis, or great muscular weakness. Thus, decay and death occur even before they would have been caused, by the impossibility of existing upon such a restricted diet.

It is worthy of notice that the central nervous system is the first to be affected by such a lack of mineral ingredients in the food.

3d. When the inorganic materials of the food are entirely withdrawn from the diet, the amount of mineral matter excreted is very much diminished during the whole of the experiment. Indeed, during absolute starvation there is more mineral matter excreted by the urine and other channels, than when the mineral ingredients alone are withdrawn and the animal is fed upon meat, (deprived of its inorganic constituents), fats and starches.

4th. The supply of those salts in the food, whose function it is to replace the salts used up in the body, may be smaller in quantity than is really needed, for a portion of the salts produced from other materials by decomposition in the body may be used to supply those nutritious materials present in the blood and secretions, which are deficient in the proper amount of saline principles.

Forster explains these results in the following manner: The greater part of the salts of the body are intimately united with the albuminoid materials. In the decomposition of these, small portions of these salts are set free and immediately excreted by the kidneys. For this reason the amount of salts in the urine is always proportional to the quantity of carbonic acid. Should there be a lack of saline matters in the food, then the albuminoids combine with the salts liberated by the decomposition of the animal tissue, and these salts are thus used over again. But, inasmuch as it takes some time to effect a chemical combination, during which the albuminoid and the salt exist free and uncombined, although near to each other, and, since decomposition and excretion are constantly going on, a diminution in the

amount of salts in the body soon sets in. During absolute starvation this takes place more rapidly because no albuminoids are introduced, which can combine with the free salts and prevent their excretion.

All of the alkalies and alkaline earths are introduced into the body through the mucous membrane of the digestive tract. In opposition to the older views it may be stated that not even water, not to speak of the alkalies or alkaline earths, can be introduced into the blood by absorption through the skin.

I.—THE ALKALIES.

PHYSIOLOGICAL ACTION.

Formerly it was generally believed that the corresponding salts of potassium and sodium had the same physiological action upon the animal body; and that it was a matter of indifference whether potassium chloride or sodium chloride, potassium carbonate or sodium carbonate were used.

It is now known however that this is by no means so, and that important distinctions between the physiological actions of the two classes of salts exist. In the body, the potassium and sodium compounds are distributed in an entirely different manner, which fact alone would suggest a corresponding difference in function. In the fluids of the animal tissues, (the serum of the blood and lymph and bile,) we find almost exclusively sodium salts, while in the blood corpuscles and in all the tissues and cells, potassium salts predominate. It is therefore possible that the sodium salts bear a definite relation to the non-organized, and the potassium salts to the organized albuminoid bodies. The traces of potassium found in the animal fluids are only transitory; they are brought here partly with the nutriment which is absorbed, and partly from the breaking up of cells. On the other hand the small quantities of sodium salts found in the ash of the burnt animal tissues are due to the residual blood serum which has been burnt with the tissues, and should not be considered as a constituent of the cell. All of the particles of potassium which get into the blood are either immediately absorbed by the cells or quickly excreted with the urine. If, in consequence of pathological conditions, or of too great an absorption of potassium the blood serum is not rapidly deprived of its potassium salts, general systemic disturbance (symptoms of poisoning) sets in. The animal cell

has an active affinity for the potassium salts and none at all for the sodium salts. The former diffuses much more readily through animal membranes than the latter, which necessitates an important distinction in the action of the two drugs.

The difference in the relations of the potassium and sodium salts to the animal economy is further illustrated by the manner in which they are excreted. This has been investigated by Salkowski, upon the human body in health and disease. Normally the excretion of the alkaline salts takes place principally through the urine ; and under ordinary conditions of nutrition in healthy persons the amount of sodium excreted is greater than that of potassium. But in disease large quantities of alkali can be excreted, with the saliva, in salivation, with the mucus of the air passages, and with the secretions of the rectum, in typhus ; and furthermore during fever, we find that the sodium in the urine is considerably less than the quantity of potassium being often diminished to the minimum, while the absolute quantity of potassium is 3, 4 or even 7 times greater than in the non-febrile state. The opinion of Salkowski that this reversal of the usual conditions is due to the more rapid oxidation of the potassium bearing tissues during fever is highly probable.

According to Rabuteau's law, that the toxic effect of the elements varies directly as the atomic weight, the alkaline metals, when classified with reference to the intensity of their poisonous effects, should be arranged in the following descending series. Caesium, (atomic weight 133) ; Rubidium, (85.4) ; Kalium, (39) ; Natium, (23) ; Lithium, (7). Caesium would thus appear as the most poisonous and lithium the least poisonous of the alkaline metals. But according to Husemann lithium, the metal having the lowest atomic weight is the most poisonous, while rubidium, the metal having the second highest atomic weight, is almost entirely harmless. Husemann therefore considers Rabuteau's law as untenable. According to him, all metallic salts of equal solubility and diffusion power produce an effect directly proportional to the amount of the metal contained in the salt ; that is, inversely as the atomic weight of the acid, provided the latter has not of itself an eminently poisonous influence. Potassium and lithium chloride, for instance, are about equally poisonous both for cold as well as warm-blooded animals. But owing to the low atomic weight of lithium, the lithium chloride contains in 100 parts only 16.37% of lithium, while in potassium chloride there *are 52.34% of potassium.* So that the toxic effect of potassium *to that of lithium as* 1:3¼. Certain doses of sodium com-

pounds are perfectly harmless, when similar doses of the potassium salts would cause the death of the animal. In 2 or 3 times stronger doses they produce a temporary faintness, and it is not until we have administered enormous doses that death follows. According to the experiments of Falck-Hermanns, injections of potassium chloride into the veins of dogs have 53 times as intense an effect as similar injections of sodium chloride.

The sodium salts injected into the blood even in large doses have no effect upon the heart, temperature, nerve centers, muscles or peripheral nerves; and it is not until we make use of very concentrated solutions that the irritability of these tissues becomes affected. The potassium salts, on the other hand, are poisonous to the heart, nerves and muscles, and produce death by paralysis of the heart. By the administration of enormous doses of sodium chloride animals may be rendered apparently lifeless and yet have the heart still beating; on the contrary in poisoning produced by potassium chloride the heart has already stopped, while the animal is still breathing irregularly. In poisoning of the warm-blooded animals with sodium chloride we often find a discharge from the mouth and nose, and atelectasis of the lungs; that is to say, changes in the organs of respiration, together with a great increase in the quantity of urine excreted. This is not found when potassium chloride has been used. So also we have a difference in the manner in which death takes place after fatal doses of sodium and potassium. (Grandeau, Guttman, Falck, etc.)

We have, then, not only a quantitative but also a qualitative difference between the relative toxic power of potassium and sodium compounds.

The relative proportion of the amount of sodium and potassium salts taken with the food is very variable. In the diet of the carnivora the amount of potassium and sodium is about equal; in the diet of the herbivora, however, the amount of potassium is much greater than that of the sodium, as will be seen from the following comparative analysis of the inorganic constituents of the principal materials of human and animal diet. According to Wolfe, we have for one equivalent of sodium the following equivalents of potassium :—

	Potassium.
Ox blood	0.11
White of hen's egg	0.65
Yolk of hen's egg	1.04
Cow's milk	1.67

Buckwheat	2.48
Lean meat	3.38
Hay	3.79
Oats	4.81
Wheat	9.36
Clover	10.42
Rye	12.18
Potatoes	15.16
Peas	28.64

Kemmerich made some interesting experiments concerning the relative nutritive value of potassium and sodium salts. He fed two dogs with meat which had been boiled twice, and thus deprived of the greater part of its salts. Each dog received equal quantities of meat treated in this way; one, however, he fed, in addition, with sodium chloride (sodium dog), the other (potassium dog) with an equal quantity of a potassium salt. After 26 days of this otherwise absolutely similar diet, the potassium dog showed a gain in weight of 2085 grms., the sodium dog of only 810 grms. According to this experiment the potassium dog had gained 1275 grms., (about ¼ of his bodily weight) more than the sodium dog. At the conclusion of the experiment, the potassium dog was a strong, lively and intelligent animal, not fat, but with a well developed muscular system. The sodium dog, on the contrary, was in a pitiful condition, scarcely able to walk, and lying for the most part in his corner, indifferent, eyes spiritless and dull, and feeding only when forced. The conditions of the experiment were now reversed, the former potassium dog now being fed with sodium, and the sodium dog with potassium, and it was found that the gain in weight was in favor of the new potassium dog, amounting to an addition of 1850 grms., while the new sodium dog gained only 530 grms.

The conclusions derived from these experiments were that a sufficient supply of potassium salts with the food enabled the organism to apply a portion of the food to the increase of the muscular tissue; while this does not take place when sodium alone has been supplied in the diet. Further experiments, however, taught Kemmerich that the muscles of the potassium dog continued to increase in size only when small quantities of sodium chloride were given with the potassium salt, the muscles remaining stationary in their development when no sodium chloride had been added. In other words, potassium *salts alone, without* sodium chloride, are incapable of causing *an increase in the* muscular tissue. This result weakens the

importance of the first series of experiments, and in addition to this, Forster has made several important objections to the experiments of Kemmerich, namely, that the results were based entirely upon a comparison of the bodily weights of the dogs experimented upon. "Voit has already shown how a neglect of the other particulars gives rise to great sources of error. The potassium dog of Kemmerich, for example, may have gained in weight, not because of an increase in the amount of flesh, but because of an increase in the amount of water; while, on the other hand, the sodium dog may have become lighter and been made ill on account of a diminution in the amount of water. As a fact, Forster found as a result of the abstraction of salt from the food, a general diminution in the amount of water contained in the different organs. If, then, we would study the influences of a diet from which salt is excluded, we must take into consideration not only the weight of the body but also the amount of carbonic acid salts excreted.

Garrod's Theory of Scorbutus.—It was believed that scorbutus or scurvy had been observed to occur as a consequence of a want of fresh vegetables, rich in potassium salts, in the diet, and upon this Garrod based the assertion that scorbutus was the result of an insufficient supply of potassium to the organism. Against the accuracy of this theory, however, we have, 1st. The fact that epidemics of scurvy have occurred when there was no lack of fresh vegetables or potatoes, as in the scurvy epidemic upon the frigate Novara, in Ingolstadt, 1871, etc. 2d. That meat contains sufficient quantities of potassium, and that the purely carnivorous animals, as well as those people who live almost entirely upon meat, do not suffer from scurvy. In addition to this, we have the fact, that there is not a single observation to prove that the blood corpuscles or muscular tissue of scorbutics are any poorer in potassium than those of healthy persons; nor is there a single observation which has determined in a reliable manner the amount of potassium excreted by the urine during scurvy. Even the suggestion of Chalvet, that the salts of potassium with the vegetable acids are more easily assimilated than the potassium chloride and phosphate of the meat, and that for this reason the former are curative in scurvy, inasmuch as they supply something that is wanting, is disproved by whole nations who live almost exclusively upon an animal diet. In addition we have the fact that almost all scurvy epidemics may be due to so many other possible and probable causes, such as *foul air, bad dwellings,* the drinking of unhealthy water, or the

consumption of putrid meat, etc., and furthermore, that the disease scurvy appears under so many different forms.

At present, then, we have not a single positive evidence which would lead to the belief that scurvy is due to the absence or diminished supply of potassium in the food or to any inability of absorption of the potassium salts on the part of the animal cell. If those tissues which are of the most importance in holding the potassium salts in combination, namely, the blood corpuscles, muscles, etc., are the ones principally affected in scurvy, it is just as proper to consider the disease as depending upon an increased consumption of potassium, as is the case in fevers, as that it is due to a diminution in the potassium supply.

The Sodium Compounds.—We shall here consider only those sodium compounds, whose influence upon the organism is mainly due to the sodium which they contain, and whose action is not much modified or entirely masked by that of their acids or other components. The latter we shall consider under the heads to which they belong by reason of their principal action, as for instance under the head of the Cyanides, Iodine, Bromine, Salicylic acid, Benzoic acid, etc.

Concerning the action of sodium administered in large doses we have observations by Bernard, Grandeau, Podcopaew, Guttmann, Hermanns-Falck, Aubert and Dehn, and Barth-Binz. We have also comparative observations, partly upon the action of sodium and potassium chlorides, and partly upon that of the compounds of sodium and potassium with carbonic, nitric and vegetable acids.

Acute Sodium Poisoning.—As we have already shown, sodium salts, administered in quantities that would be fatal doses of potassium salts, whether injected subcutaneously or into the veins, produce no effect whatever upon the animal body. Indeed dilute solutions of sodium chloride (0.75 %) or sodium phosphate preserve the irritability of nerves and muscles that have been cut out of the body, while similar solutions of potassium chloride destroy it. Striped muscular tissue which has had its irritability destroyed in weak potassium solutions, will have it restored when placed in dilute sodium solutions. Even muscles that have been stiffened in *rigor mortis*, when placed in a 10% solution of sodium chloride, have their acid reaction neutralized, and their condition of coagulation altered, so that they again regain their elasticity and the color of living muscular tissue, without of course having the properties which characterize them during life restored. Naturally, however, there is

a limit even for the sodium compounds beyond which their action upon the organism is injurious and destructive.

According to the statements of several authors, the only symptom produced by large but not fatal doses is a temporary faintness, without any or very slight disturbance of the heart, respiration and temperature. Even fatal doses kill very slowly. Warm-blooded animals, after an injection of 5.0 grms. of sodium nitrate, become very quiet, weak, and die in the course of half an hour to an hour, without any severe disturbances in respiration; the heart beats almost to the last, with normal frequency and force. The slight weakening in the force of the heart's contraction, Guttmann considers the result, not of the sodium action, but of the empty condition of the blood-vessels due to a diminution in the amount of water contained in the blood. The temperature does not vary. Convulsions do not occur, and the central nervous system, as well as the muscles and peripheral nerves, show no changes worthy of mention.

The results of these experiments of Guttmann's leave it still doubtful, as Guttmann himself acknowledges, as to what is the real cause of death. For death can only follow as a result of the abolition of the function of some organ necessary to life, and this should certainly follow here, if we are really to believe that the principal cause of death is the abstraction of water from the organs.

There must have been something overlooked, and we must consider this problem as not yet entirely solved. In addition to this we have the fact that very recently Aubert and Dehn have declared that the injection of sodium salts into the blood even in small doses produces an effect upon the action of the heart similar to that produced by potassium.

Nor can the abstraction of water from the cells be the only cause; for rabbits die from sodium even when water is constantly injected into the stomach; in like manner frogs, even when the body is kept immersed in water or when a quantity of water five times greater than the quantity of sodium solution is injected under the skin of the back. We must consider then that the altered composition of the blood, by the great increase of the amount of sodium contained in it, is an important factor in this poisoning. (Guttmann).

Deutschmann and Heubel have thoroughly studied the fact, which was *first observed by* Kunde,* namely that the crystal-

* Compare Sod. Chloride.

line lens becomes clouded under the influence of sodium chloride, with the following results. This cloudiness can be produced in cold and warm-blooded animals, not only by sodium chloride but by a large number of other water abstracting salts, and other substances, as for example, all the possible salts of sodium, potassium, ammonium, magnesium, barium and strontium, as well as sugar and uric acid. It is not then a specific effect of the sodium. The only cause of this cataract-like cloudiness is an abstraction of the water from the lens brought about by osmotic action. These substances in solution possessing an affinity for water, are brought by diffusion into the aqueous humor and vitreous body, where they are separated from the water contained in the lens only by the lens capsule; the result is that small amounts of these solutions pass into the lens while larger quantities of the fluid in the lens pass out. We can, however, only produce this cloudiness in the lens in cold and warm-blooded animals, by placing any of the above substances directly in contact with the conjunctival sac of the eye. Should these substances be introduced under the skin or into the stomach, then most of them will produce no evident influence upon the lens. Sodium salts only, namely, the chloride, the nitrate, the chlorate, the sulphate, the sulpho-tartrate, the hypo-sulphite, the tartrate, the bromide, the carbonate and the bi-carbonate, and of the organic materials, sugar, *in the order in which they are stated*, sodium chloride being the most powerful, produce, after subcutaneous injection, a *cloudiness in the lenses of frogs.*

Other sodium salts, such as sodium iodide, phosphate, biborate, acetate and salycilate yielded only negative results. The reason why the sodium salts, introduced subcutaneously or by the stomach, cause a clouding of the lens, is as follows. The salts of sodium can be taken up by the blood in relatively large amounts without sensibly affecting functions important to life. If, on the one hand, the absorption of some sodium salts, such as the phosphate and carbonate, proceeds rather slowly on account of their low diffusion power, they are not as readily, on the other hand, excreted from the blood, as are, for instance, the potassium salts. The sodium compounds are thus enabled to collect in the blood in larger quantities, and therefore appear in larger amounts in the transudations; as for instance in the aqueous humor, from which they pass into the lens.

The difference in the action of the various sodium *compounds depends partly* upon the difference in their diffusion

power, (see chapter on the difference in action of the individual potassium compounds) and partly, perhaps, on the fact, that in some sodium salts the acid component interferes to some extent with the purely sodium action; as is supposed to be the case by Barth in sodium nitrate, and by Marchand in potassium chlorate. We should however, go too far, were we to consider, on account of these slight differences, that sodium has no physiological action; for this action will always have to be taken in consideration in comparing the physiological action of the corresponding sodium and potassium compounds.

Chronic Sodium Poisoning.—Apart from the doubtful statement that scorbutic symptoms have been observed to follow the long continued use of, for example, sodium bicarbonate, we have only the single series of experiments made by Lomikowsky upon dogs, in which the functional and anatomical alterations following upon the administration during several weeks of 150–600 grms. of bicarbonate of sodium, were studied. The doses given at a time with the food, varied from 1–5.0–60.0 grms. As early as the 3d–5th day vomiting, fluid stools, diminished appetite, and the excretion of strongly alkaline urine, set in. The animals grew more and more lean every day, and this to such an extent that the experiments had to be interrupted from time to time until the animals had slightly recovered. *Post Mortem* the following changes were found:—a swelling and infiltration of the gums; fatty atrophy of the heart; anemia of the liver, spleen and lungs; in the intestinal canal particularly, there were changes, a hyperplasia of the Peyer's patches, and solitary glands; in the spleen, enlargement of the Malpighian corpuscles, caused by an infiltration of lymphoid elements. None or very little sugar was obtained from the liver. It is necessary that more accurate and complete experiments should be made concerning this subject.

The Potassium Compounds.—As was the case with the sodium compounds, so with most of the potassium compounds, the carbonate, the combinations with vegetable acids, the phosphate, the nitrate, and the chlorate, we find a similarity of action upon the animal organism, which we shall term the potassium action, because it is produced by the potassium present in these compounds.

This common potassium action is modified according to the acid which is joined to the base; either, only slightly, as is the case with acids above named, or more strongly, where the other component is iodine, bromine or sulphur, or as in potassium cyanide, potassium arsenite and the tartrate of antimony

and potash, the modification is so powerful, that we perceive only the action of the hydrocyanic acid, the arsenious acid, and the antimony, while the potassium effect is entirely lost. We shall therefore consider under the head of potassium compounds only the first named salts, (carbonates, salts of the vegetable acids, etc.,) while the remaining compounds will be treated of under the head of iodine, bromine, sulphur, antimony, hydrogen cyanide, etc.

The Poisonous Effects of Potassium.—Ever since it has been determined with certainty that the potassium compounds are fatal to life in much smaller doses than the corresponding sodium salts, the poisonous nature of the former has been dwelt upon with too much solicitude. It is, therefore, above all, necessary that the whole matter be properly represented. In this connection Bunge points to the large percentage (0.2–1.9) of potassium contained in most of the articles of food, as tending to prove, that not inconsiderable amounts can be taken without harm. According to Bunge, with every pound of white bread we receive 1.3–2.7 grms. of potassium; in every pound of meat 2.7 grms., in every liter of beer 1.0 grms. A meal consisting of 1 pound of meat and 2 pounds of potatoes, which can not be considered too much for a laborer, introduces into the body 11.0 grms. of potassium, that is to say 20.0 grms. of a potassium salt (maximum calculation). According to Buckle an Irish laborer consumes daily, on an average, 4309.0 grms. of potatoes, and this amount contains, according to Moleschott, 21.0–38.0 grms. of potassium, equal to 40.0–70.0 grms. of a potassium salt, which is taken into the body daily.

Bunge compared the conclusions of all the experimenters and finds:

1. When introduced through the stomach, the following doses were fatal:

In the rabbit 3 grms. potassium chloride in 30 minutes: 1–2.5 grms. K_2O as K_2H Po_8 equal to about 1.6–4.0 grms. KCl in 40–70 minutes; in dogs which were 6 kilograms in weight, 16–20 grms. KCl. in 60 minutes.

2. When injected under the skin:

In the rabbit 1.0–1.5 grms. KCl, KCO_3 and KNO_6 in 15–20 minutes; when 1200–2000 grms. in weight, 4 grms. KCl or KNO_6 in 47–350 minutes. In cats, 8 grms. in 75 minutes.

3. When directly injected into the blood:

In rabbits, 0.23 grm. KCl; in cats 0.1 KNO_6; in dogs 0.3 *grm.* KNO_6; *0.1–1.2* KCl.

From this table we conclude that potassium salts only act as

more intense poisons, when injected directly into the blood, whence passing into the jugular vein they are soon enabled to exert their influence directly upon the heart. If hypodermically injected or introduced into the stomach, even small animals require very large doses to produce a fatal effect. Were it proper to draw a conclusion from the amount necessary to kill a rabbit, as to the fatal dose for a man, we would find that, since a rabbit, weighing 1 kilogram, is killed by the administration by the stomach of 3.0 grms. of KCl, a man 75 kilograms in weight would require 225 grms. of potassium salt as a fatal dose. But the quantity is certainly too large—for a man is differently affected by drugs than a rabbit, apart from the fact, that experience has shown that most poisons do not exert an effect proportional to the weight of the body, but that the fatal doses increase to a less extent than would be warranted by the increased weight of the body. Were we, however, to take 50 grms. as the fatal dose for a man of the given weight, even then death from paralysis of the heart would not take place from potassium salt introduced into the stomach, since experience teaches that so large a quantity is immediately expelled by vomiting, while the portion that has passed into the blood is rapidly excreted with the urine. It seems then exceedingly difficult to affect the action of the heart in man, by the introduction of potassium through the stomach, and it is only after long and continued use of proportionately large doses that any signs of heart weakness can be observed. When men or animals die from the introduction of potassium salts into the stomach, it is generally caused by a local gastro-enteritis, due to the action of a very concentrated solution, rarely, and perhaps never, by a direct paralysis of the heart.

The Influence of Potassium Upon the Functions of the Human and other Animal Bodies.—Under this head we shall consider, not the local effect of concentrated solution, but the general effect of potassium solutions absorbed into the blood.

Large doses of potassium can with difficulty be administered to men, dogs, and cats, inasmuch as they are immediately vomited. In most of the experiments, therefore, the drug was injected hypodermically, or into a vein, rarely into an artery.

Central Nervous System.—The potassium salts have a directly paralyzing effect upon the central nervous organs of cold-blooded animals only. And in these, paralysis of the heart and spinal cord with loss of sensibility, motor power and reflex irritability occur simultaneously. The irritative and paralytic disturbances of the brain and spinal cord of warm-blooded

animals, on the other hand, are due, as will be seen later on, to the weakness and paralysis of the heart.

Peripheral Nervous System and Voluntary Muscles.—In consideration of the exaggerated opinions, which generally prevail, concerning the evil effect of the potassium salts upon the muscles, it seems necessary to affirm the correctness of the results of Guttmann's experiments; according to which the potassium salts, even in one per cent. solution, do indeed exert a deleterious influence upon the muscles and peripheral nerves when separated from the body; but in the living body, while circulating in the blood, they have only a slight effect upon the muscles, and none at all upon the nerves; in warm-blooded animals there is no effect produced, even upon the muscles.

Even enormous doses of potassium injected into the veins, produce no muscular paralysis in warm-blooded animals. For the heart's action is so quickly arrested that the poison has no time to affect the muscles.

The rapid death of muscles and nerves, which have been cut out of the body, and placed in solutions of potassium, can only be due to the abstraction of the water from the tissue, and not to any chemical change, since the same preparations placed in sodium solutions of a similar strength, remain unaffected.

From the foregoing facts, the following theory of the action of potassium upon the muscles can be formulated: That, since potassium is a constant ingredient of the muscular cell, and since depriving the body of potassium diminishes the amount of muscular tissue formed, therefore it must be considered as a necessary component of muscular tissue. Buchheim, indeed, supposes that the contractile substance of muscle is a molecular compound of an albuminoid material with a potassium salt; and that by too great a supply of potassium this is changed in its composition, and loses its former characteristics. To prevent these evil consequences upon the muscles the living organism is so constituted that enormous doses of potassium, when introduced into the stomach, have great difficulty in gaining access into the interior of the body; and even if they are absorbed, are rapidly execreted with the urine.

Muscular Apparatus of the Stomach and Intestines.—Under the influence of large doses of potassium these muscles very rapidly lose their irritability; and this from the same causes that affect the voluntary muscles, when placed directly into solutions of potassium. For here there is a more concentrated and direct influence; the potassium salt reaching the muscles

of the stomach and intestine, less diluted, than when they come in contact with the more distant muscles of the extremities. Perhaps this is the cause of the frequent digestive disturbances which we find after long-continued use of 2–3 per cent. solutions of potassium salts.

Circulatory Apparatus.—In cold-blooded animals after the direct introduction of potassium preparations, the heart's action is weaker and slower; that is to say, the systole is often twice as long as the diastole. Final stoppage of the heart can be rapidly produced by large doses.

Kemmerich states that in rabbits the potassium salts affect the nerves of the heart in such a manner as to produce an increase in the rapidity of the heart's action. Bunge, on the other hand, believes that he has found a similar quickening of the heart's action in rabbits after the injection of warm and cold water, and solution of sugar, and of sodium salts, and considers it, therefore as rather the result of fear and excitement; further, that in other animals, (man, dog and cat) the absorption of potassium salts does not produce a quickening of the pulse.

For reasons given above, Mickwitz made no experiments upon the action of potassium upon the heart, when given by the stomach, nor when introduced by subcutaneous injection, for this also produced accessory disturbances. But, in the interests of theoretical pharmacology, he made his injections into the jugular veins of normal cats, and also of some under the influence of curara, and found the following effects upon the heart: 1. Small doses (0.05 grm.) of potassium nitrate produce a slight lowering of the blood pressure with very little slowing of the pulse; this is followed by a rise in the blood pressure with an increase in the rapidity of the pulse. While this increased blood pressure is still present, a slowing of the pulse again takes place, which persists, while the blood pressure falls back to the middle point. 2. Large doses (0.2 grm. and over) cause immediately, and sometimes while the injection is being made, a diminution in the blood pressure, and in the frequency of the pulse and death by paralysis of the heart.

According to these findings, the observations of all the previous observers, under certain limits, were correct, and the inconsistencies are only due to the varying sizes of the doses administered; both Traube, who observed that an injection of potassium nitrate to the amount of 0.12 grm., in dogs, was followed by a rise in the blood pressure, with diminution of the frequency of the pulse, and Bunge, according to whom the p

death from potassium in the mammalia is caused by the rapid sinking of the heart's action and the final stoppage of the heart. This action upon the heart results secondarily in the dyspnœa caused by the diminished interchange of the gases of the blood, and in clonic convulsions, which again are the result of the diminished interchange of the gases of the blood, and also of the diminished blood supply to the brain. In cold-blooded animals, which can live for a time with a dead heart, or even none at all, the rapid death is produced by the stoppage of the heart together with a paralysis of the nerve centers.

DIFFERENCE IN THE ACTION OF INDIVIDUAL POTASSIUM COMPOUNDS.

Within the limits of the action which has just been described as common to all of the potassium salts, we find the other component of the different salts, that is to say the acid, producing variations in their action.

Buchheim has attempted to explain this variation partly by a difference in the diffusion power of the various salts. For the potassium salts, like the sodium salts, which as a rule are of a lower diffusion power, vary in the rapidity of their diffusion according to the acid with which they are combined. The potassium bicarbonate, phosphate and sulphate are the slowest, the iodide, bromide, and chloride more rapid.

Inasmuch as the potassium salts of lower diffusion power are taken up more slowly by the blood a larger amount is enabled to collect in the small intestine, and here exert a cathartic action, like that of the sodium sulphate, for instance. These salts irritate the intestinal nerves, in consequence of which the peristaltic action is hastened, the solutions of the salts are carried rapidly to the end of the intestinal canal and discharged before there has been time for their absorption. We therefore find only a portion of the cathartic salts in the urine, since the other part is discharged by the feces.

When, however, we bring an easily diffusible potassium salt in contact with a very vascular animal membrane, then the arterial pressure in the capillaries is overcome by the intensity of the diffusion current. Since the fluid of blood is exchanged for unequal quantities of the potassium salt solution, the blood corpuscles must collect in large quantities in the capillaries, we therefore have toxic inflammation of the stomach, ecchymoses of the mucous membrane, pain and vomiting following the in-

troduction of these salts into the stomach. And since the absorption into the blood takes place rapidly, whether gastritis sets in or not, but little of these substances enter the intestine and no diarrhœa results. Filling the stomach with food, or extensive dilution of the potassium salt will also greatly affect the diffusion power; for this reason sometimes larger and again only smaller amounts can be borne. Potassium nitrate and oxalate most frequently produce an inflammation of the stomach, more rarely the bromide, iodide, and chloride.

But not only is the diffusion power of great importance to an understanding of the stomach and intestinal action of potassium salts, but also for a comprehension of their general behavior. For it is only by a consideration of the diffusibility that we can explain why, notwithstanding the large and often varying quantities of alkali contained in the food, the supply of potassium salts to the blood never oversteps certain limits. The materials of food contain only the potassium salts of low diffusion power, and only small quantities of the easily diffusible potassium oxalate, nitrate and chloride. Absorption of an amount of potassium salts injurious to health can therefore only take place when large doses of potassium oxalate, nitrate, chloride, bromide and perhaps also the iodide, are introduced into the empty stomach. These salts only, then, can be used, therapeutically, to affect the heart's action. The other potassium salts would be of no avail even in large doses.

Theory of the Action of Cathartic Salts.—There has been much dispute concerning the cathartic action of the sulphates, etc., of the alkalies and alkaline earths.* The above view of Buchheim, which holds good for the sodium as well as the potassium salts, appears to us most easily to unite the contradictory results of experiments. We shall here again give a synopsis of the different opinions. Poiseuille, Liebig and others believed that when a concentrated solution of a salt is introduced into the intestine, according to the laws of endosmosis, more fluid passes out from the fluid of the blood, which is poor in salts, than passes in; by which, naturally, the amount of water contained in the intestines is increased and the stools rendered more fluid.

On the other hand Aubert observed the fact, also acknowledged by Buchheim, that even after enormously diluted solutions of Glauber or Epsom salts, the same cathartic action followed as when the solutions were concentrated and contained

* Compare the cathartic acids.

much salt. Aubert, therefore, rejecting the Poiseuille-Liebig theory, believes the cathartic action to be caused by an increased peristalsis due to nerve irritation.

Buchheim injected 50.0 grms. of Glauber's salts into the jugular veins of dogs, and found that not only did the stools not become fluid, but that the feces even became drier than normal. The cathartic action, therefore, following the introduction of these salts into the stomach, cannot depend upon an irritation of the nerves of the intestine, for then we should have expected a similar irritation when the salt was injected into the blood, and diarrhœa should have followed. But that even strongly diluted solutions of Glauber's salts are very slightly absorbed, Buchheim showed by comparing the amount of sulphuric acid contained in the urine and feces; indeed he found that large dilution rather retarded than increased the absorption of Glauber's salts into the blood. We cannot, therefore, consider that the increased amount of water contained in the feces is dependent upon an increased excretion of water from the intestine as Liebig believes, since a similar effect follows the use of greatly diluted solutions of Glauber's salts; but that it depends upon a retention of the fluid in the intestines on account of the diminished absorption of the same, which is caused by the low diffusion power of Glauber's salts. In favor of this latter conclusion we have the fact that the more easily diffusible sodium chloride, even in similar concentration, does not exert a strong cathartic action, as do Glauber's and Epsom salts. The increased peristaltic action, which Buchheim does not deny, may be the result of the presence of a large amount of foreign substances in the lower portion of the intestinal canal, without supposing these substances to possess any peculiar action upon the nerves of the intestine.

Against the view of Buchheim we have the undoubtedly accurate experiments of Voit, Bauer, Moreau, Lauder Brunton and Brieger, who placed Glauber and Epsom salts in isolated portions of the intestine, and soon saw a considerable amount of fluid material collect in them. Thiry, who performing a similar experiment under the same conditions, did not succeed by the use of concentrated solutions of Epsom salts in causing any transudation into the intestine, evidently failed because he allowed the injected solution to come in contact with the mucous membrane of the intestine for only a quarter of an hour. But, as Heubel properly objects, Brieger's experiments do not *prove that which they* are meant to prove, namely that the cathartic salts, under ordinary circumstances, and after their in-

troduction into the stomach, act as Brieger believes they do. For it is an entirely different matter whether a salt enters the body, by being introduced into the stomach with more or less water and then passes through the whole length of the intestine, which generally contains much fluid, or whether the same salt has been inclosed in an entirely empty portion of the intestine tied at both ends. In the latter case the salt, in order to satisfy its affinity for water, must necessarily obtain the water from more difficult sources, namely, from the blood, while in the former case, naturally, the water contained in the stomach and intestine, which is easiest of access, is used for the same purpose. We would then only expect the cathartic salts to produce a transudation of water from the blood through the wall of the intestine, where circumstances similar to those under which the Voit-Brieger experiments were made, happened to be present in the intestine; that is to say, when concentrated solutions of the salts were detained by some mechanical obstruction, as, for instance, hardened feces in a fixed position in an intestinal canal containing but little fluid.

We therefore believe that Liebig's theory can be maintained without rejecting Buchheim's experiments. Buchheim has also shown that the cathartic salts have a cathartic action even when, on account of the great dilution of the solution, there is little difference between the amount of salt contained in the blood and that contained in the intestine, and that therefore these do not act entirely in the manner explained by Liebig.

The Lithium Compounds.—Husemann has studied the physiological action of lithium chloride by preference, but also that of other lithium salts. The officinal lithium carbonate, however, he has only slightly studied, because it is not fitted for subcutaneous injection, an account of its insolubility. He found that the lithium salts, like those of potassium, when given in large doses rapidly introduced into the blood are cardiac poisons both in cold and warm-blooded animals, as in the frog, rabbit and pigeon; and that they produce a slowing of the pulse and finally a stoppage of the heart, while the nerve centers and periphery as well as the striped muscular fibers still retain their irritability, and reflex movements can still be effected. The irritability of the heart to electricity is abolished immediately after the stoppage of the organ. Before this has taken place irritation of the vagus aften causes temporary diastolic intermissions, which cease when the animal has been placed under the influence of atropia, or the vagus has been

divided. Neither the central nor peripheral nervous system nor the muscular system remain intact under the direct application of lithium; in frogs, the strychnia convulsions can be suspended by means of lithium. Great reduction in temperature results from toxic, even if not fatal doses of lithium; and a diuretic effect has also been observed.

In cases of poisoning due to the caustic preparations of potassium and sodium—and the same rules hold good for caustic preparations of ammonium and calcium—the first therapeutic indication is to neutralize the caustic base. For this purpose harmless acids are to be preferred, of which the best is vinegar, which is everywhere to be obtained and in the absence of which lemon juice will suffice. A patient thus suffering from poisoning can drink vinegar and water. Should these acids not be at hand we may attempt a saponification, and for this purpose administer any fats or oily substances that may be obtainable. The treatment of the resulting inflammatory symptoms, and the collapse, is the same as that of any other toxic gastritis.

I.—THE CAUSTIC ALKALIES.

LIQUOR SODII HYDRICI SEU CAUSTICI.

Solution of caustic soda. A solution of 20 parts of sodium hydroxide ($Na\ OH$), in 100 parts of water, is a clear, colorless or slightly yellow fluid.

This preparation is little used because it is believed to exert an exactly identical local effect to that of the solution of caustic potash, that is to say, its caustic effect is similar; and, by accident, the caustic potash preparation only is therapeutically used.

The dosage and manner of application is the same as that of the corresponding potassium preparation.

POTASSIUM HYDRICUM S. CAUSTICUM.

The caustic alkali, potassium hydroxide (KOH) can be used under three forms.

1. Potassium hydricum solutum. Liquor pot. hydrici. Potassium solution. 33 % of potassium hydroxide in water.

2. Potassium hydricum siccum (the foregoing preparation which has been evaporated.)

3. Potassium hydricum s. causticum fusum),—caustic stone of surgeons—(preparation No. 2, cast in cylindrical rods.

The last two preparations are very deliquescent and absorb carbonic acid from the air, thus forming a potassium carbonate, and must therefore be kept well protected from the air.

PHYSIOLOGICAL ACTION.

The action of these preparations in concentrated condition consists of a very powerful caustic effect upon animal tissues,

and depends upon the abstraction of water from these, upon an extensive alteration of the albuminates and partly upon a saponification of the fat; the coagulated albuminates are dissolved; these, together with the combinations of the liberated albuminates which act as bases to the alkalies, are finally replaced by the formation of ammonia, leucin, potassium sulphide and other substances.

When brought in contact with the skin, these preparations first soften the epidermis, and finally destroy, with great pain, the structure of the tissues, far beyond the point of application; a slough which is at first hard and then soft is formed, and is finally thrown off. The scar is extensive.

Internally administered they destroy all of the mucous membranes with which they come in contact, changing them to a soft slough, and setting up an inflammation in the deeper tissues. The symptoms of internal poisoning are great pain in the mouth, pharynx and œsophagus, terrible pain in the abdomen, excessive vomiting and diarrhœa and death. The latter is the result of the toxic inflammation of the stomach and intestines, or of perforation of the stomach and intestinal wall, and resulting peritonitis. Should the patients not die, there remain persistent gastric catarrh, and strictures, especially of the œsophagus, with the resulting consequences, namely starvation, etc.

In sufficiently strong dilution so that no caustic effect ensues, the action is the same as that of potassium carbonate.

THERAPEUTIC APPLICATION.

Caustic potassium is not used internally at all, inasmuch as in sufficient dilution, and only such solutions could be used, the effect is the same as that of potassium carbonate, while it interferes with the digestive functions more than this salt. On the other hand, it is extensively used externally, and has many advantages as a caustic over other caustics. It is used when it is necessary to produce an energetic and deep destruction of tissues, and when a careful limitation of the caustic effect is not necessary.

Caustic potash, then, would be the best caustic to use for the wounds caused by the bites of mad dogs, and for other wounds infected by animal poisons, as also for snake bites. Further, it should be used when certain portions of tissue are to be entirely destroyed, as for the destruction of hardened edges of ulcers or tissues which have undergone a lupoid degeneration.

For lupus, R. Volkmann considers it the best caustic next to the nitrate of silver, provided that it is proper to use a chemical caustic.

In applying it to the face great care is necessary, for cosmetic reasons.

If we wish to produce an adhesive inflammation in the deeper tissues by means of a chemical caustic (Récamier's method) as for example between the layers of the peritoneum, in order to open abscesses of the liver, echinococci cysts, hydronephrosis, etc., we may make use by preference of potassium hydrates.

To open peripheral abscesses a surgeon would hardly dare to use the caustics either for "anatomical reasons" or because the patient feared the knife. In inveterate cases of eczema, that have withstood all other methods of cure, we may according to Hebra use a 50 % solution of potassium as a wash repeated once a week often with certain result. Every application of potassium hydrate as a caustic is very painful.

In dilute solution the caustic potash is used for external application, washes and local baths, simply to produce an irritation of the skin, but the same effect can be produced more safely with solutions of potash. To-day no one would attempt to cause the disappearance of neoplasms by applications of potassium hydrate, as was formerly advised. For scabies we now have better remedies.

Dosage and preparation.—1.—Potassium hydricum for internal use, the dosage is unnecessary since it is practically not used. Externally as a caustic in substance (pot. c. fusum): the usual procedure is either to apply the caustic when held in the hand by means of a caustic holder or some instrument of that kind, or the potassium is placed upon a small piece of adhesive plaster with an opening in the center, so as to prevent the spreading of the effect over the skin. For washes and local application the strength is 10.0–20.0 to 500.0 of water. For local baths 2.0–4.0 to 1 liter of water. Pot. c. solutum in proportions twice as great.

Pasta caustic aviennensis—Vienna paste—5 (or 6) parts of caustic potash with 6 parts of caustic lime. Immediately before application the powder is made into a paste with a little alcohol, or it may be applied in substance. Surrounding the paste with adhesive plaster is a necessary precaution. It is allowed to remain in contact with the part from 5 to 30 minutes according to the locality of the disease and the effect desired.

2.—THE ALKALINE CARBONATES.

SODIUM CARBONATE AND BI-CARBONATE.

The pure crystallized sodium carbonate.—Sodium carbonate ($Na_2CO_3 + 10H_2O$) presents transparent, colorless and easily dried crystals of an

alkaline taste, ready solubility (in ¼ part of hot and 2 parts of cold water. When the water is driven off by evaporation we have the so-called dried sodium carbonate remaining. ($Na_2\ CO_3+H_2\ O$.)

The bi-carbonate of Sodium.—Hydrosodic carbonate ($Na\ H\ CO_3$) is a white crystalline powder of very weak alkaline taste, not changing in the open air, and soluble in 13 parts of cold water.

PHYSIOLOGICAL IMPORTANCE AND ACTION.

It is highly probable that the largest part of the carbonic acid of the blood and lymph is in union with alkalies (sodium carbonate and bi-carbonate.) The opinion formerly held that the sodium bi-phosphate ($Na_2\ H\ PO_4$) could unite with the carbonic acid present in the blood serum, and that the phosphates, like the carbonates, were carbonic acid carriers, is no longer tenable inasmuch as the serum of the blood does not contain sufficient alkaline phosphate, when we take the proportion of lecithine into consideration, to suffice for this purpose.—(Sertoli.)

In the introduction to the alkalies * we have already fully considered the importance of the supply of alkalies to the organism, their influence upon the solubility of the albuminates, and the increase of the oxidation processes, and will only add here, that these latter are considered the cause of the diminution and sometimes even of the disappearance of uric acid from the urine, which has been observed under the use of sodium carbonate, at least during the commencement of its action. In consequence of the increased oxidation we have the uric acid converted into urea, even in the body. However an increase in the amount of urea excreted, corresponding to the increased tissue metamorphosis, has not yet been proved.

Considering the slow absorption of the carbonates and their rapid excretion with the urine, it is not very probable that the medicinal administration of these salts can produce an alkalinity of the blood or increase the oxidation processes in the body; at least we have as yet no exact proof of this. For this reason the treatment of excessive deposition of fat, and of diabetes, by the use of alkaline waters, a method of treatment based upon the above ideas still rests upon a very uncertain basis.

Skin.—In addition to the cleansing effect upon the skin which is the result of the saponification of the oily matters of

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* See pages 9–11.

the skin combined with the dirt, concentrated solutions cause a hyperæmia and even a slight burning of the skin. It has also been supposed that since the urine becomes alkaline in reaction, that absorption can take place through the skin (in alkaline baths) but this is certainly not true.—(Röhrig.)

Mucous Membrane and Mucus.—The mucous membrane of the mouth, pharynx and stomach can be burnt by very concentrated solutions, and as a result we may have ulcers of the œsophagus and stomach, inflammation of the stomach, strictures of the œsophagus, and following these, death.

When administered in greatly diluted solutions, we see upon all of the mucous membranes, especially upon those of the respiratory tract, an increased secretion of fluid mucus or a softening of inspissated mucus; the latter is the result of a quality which all alkalies possess, namely, the power of dissolving mucin, which in ordinary water only swells but does not dissolve.

The loosening of the expectoration which is so often observed in diseases of the respiratory organs is partly due to the cause just mentioned and partly because the ciliary movements of the epithelial cells upon the mucous membrane of the respiratory tract are excited and hastened by these salts.

Gastro-Intestinal Tract. The carbonate, introduced into the stomach in a diluted condition, is partly, or, if the quantity be small, entirely changed by the hydrochloric acid of the stomach into sodium chloride, or by means of the lactic acid into sodium lactate, and partly absorbed into the blood as a carbonate. As a result of this process, the free acid of the stomach is bound, and a neutralization of the gastric juice takes place, while at the same time a certain amount of carbonic acid is liberated, especially if the salt administered was the bicarbonate, so that a part of the effect is due to the action of the carbonic acid (refer to this). The newly formed lactates, after being absorbed into the blood, are again changed to carbonates. As to what becomes of the sodium chloride and its function in the process of nutrition, we shall learn when we come to consider this salt.

Under the influence of the alkaline carbonates internally administered, there is a tendency to an increased secretion of gastric juice, so that a complete neutralization of the gastric juice can scarcely be attained; and if the salt be administered for too long a period, the direct opposite of the original intention results, and we have an excess of acid formed.

In small doses then, the constant production of sodium

chloride has a good effect upon the digestion of the albuminoids, and the increased production of the gastric juice leads to an improvement of the appetite and digestion. Haidenhain has shown that pancreatin will dissolve coagulated fibrin the more readily, the more sodium carbonate is added, until a certain limit is reached, then the dissolving power remains constant for a time, to be again diminished as the degree of concentration of soda becomes excessive. This limit varies with the quantity of pancreatin present. The larger the amount of the latter, the smaller the amount of soda necessary to lower it. For a medium amount of ferment the limit above spoken of is at 0.9–1.2 %. The cause of this increase in the dissolving power, brought about by soda, is partly the fact, as has been shown by Kuhne, that pancreatin first changes the fibrin into an albuminate, soluble in salt solutions, before the peptonization is completed. The use of that salt in disease reveals other good and valuable properties. In difficult digestion and slow transformation of the materials of food that have been introduced, some of the products of decomposition, such as the lactic and fatty acids, are neutralized by combination with the sodium carbonate. When the mucous memdrane of the stomach is covered with large masses of mucus, these will be dissolved by the same alkali.

The sodium bicarbonate is absorbed into the blood very slowly, on account of the low diffusion power; and when larger doses are administered, a portion may get into the small intestine and act as a cathartic.

Bile.—Concerning the effect upon the excretion of the bile, we have few useful observations. According to Nasse, large quantities of alkali diminish the excretion of bile (observations on dogs with a fistula of the gall bladder).

Urine.—The urine becomes alkaline under the administration of sodium carbonate. The alkalinity lasts for a greater period, the greater the quantities of alkali administered; it sets in most rapidly when the alkali has been taken upon an empty stomach. Most observers, especially Muench, agree that the excretion of the urine is increased, provided that no increase in the intestinal secretion takes place. The cause of this increased excretion is as yet unknown.

The nervous system, circulatory organs and temperature are not affected.

THERAPEUTIC APPLICATION.

Inasmuch as all of the alkaline carbonates and salts of the

alkalies with vegetable acids are of almost the same therapeutic value and used in the same diseases, it seems advisable to take up the therapy of all of these together, and we therefore refer to this article (page 42 and following) for the therapeutic application of sodium carbonate and bicarbonate, which are the most used of all these preparations.

DOSAGE AND PREPARATIONS.

1. Sodium bicarbonicum.—This is almost exclusively used internally, but the dosage for the simple salt is the same : 0.2–2.0 per dose (10.0 per day), in powder or solution, with an oleo-saccharum as the pleasantest corrective. Pills are entirely inert.

2. Sodium carbonicum crudum.—Only used externally for washes and baths, 500–1000.0 for a general bath, 100–200.0 for a foot bath. For local applications 10–30.0 to ¼ kgr. ; for ointments 1 part to 8 parts of lard ; for injection, 5–10.0 to the kgr.

3. Sodium c. purum.—Also best used externally like the crude salt.

4. Sodium c. siccum—like the foregoing. The three last preparations could easily be dropped from pharmaceutical use without any harm.

5. Trochisci sod. bicarbonici.—0.1 of the salt to each troche weighing 1.0. In a similar manner the troches of Vichy, Ems and Bilin can be used.

6. Pulvis aerophorus.—Effervescing powders. 10 parts of soda bicarb., 9 parts of tartaric acid, 19 parts of sugar ; take a teaspoonful dry upon the tongue and follow with water.

7. Pulv. aerophorus anglicus (pulveres effervescentes U. S. Ph.).—English effervescing powders—Soda powders. 2.0 Sod. bicarb. (usually in colored paper), 1.6 Tartaric acid (in white paper), dissolved in water and taken while effervescing.

8. Pulv. aerophorus laxus—Aperient effervescing powders — Seidlitz powder. 7.5 Potassium and sodium tartrate, 2.5 Sod. bicarb. ; 2.0 Tartaric acid. One or two of these as a laxative—to be taken like the ordinary effervescing powders.

9. Aquæ Sodæ—Soda Water. Artificial water containing sodium carbonate and carbonic acid. A well-known drink.

10. Saturationes.—Medicinal preparations which we could easily do without. They consist of a solution of a simple alkaline carbonate (generally potassium, more rarely sodium), in water, with the addition of an organic acid, which is stronger than the carbonic acid, such as acetic, citric and tartaric acids. The saturating proportions are as follows :

1 grm. pot. carbon. pur. ;	18.0 vinegar;	1.0 acid citric;	1.1 acid tartar.
1 grm. sod. carbon.	9.0	0.5	0.5

For example :

Potassii carbon. puri	10.0
Acid tartar,	11.0
Elæos. fœnio	30.0
Aquæ dest.	150.

11. Alkaline mineral waters.—These are divided into two groups :

(a) Simple alkaline springs—which contain as active ingredients, in addition to the alkaline carbonate, carbonic acid in smaller or greater quantity, and only traces of other substances (sodium chloride, magnesium and potassium carbonate, etc.) ; these are classed under the alkaline acid springs, on *account of the carbonic acid.*

(b) The alkaline muriatic springs—in which, in addition to the alkaline

and carbonic acid, we have considerable amounts of sodium chloride as an active ingedient.

1. Vichy—Dep. Allier in France. A series of springs with water having a temperature of 12–45° C.; the warmest are the Grand Grille, Puits Chomel, Puits Carre. Up to 0.5 sod. bicarb. 2. Neuenahr in Ahrthal; warm springs 30–40° C., containing about 0.1 % sod. bicarb. The following springs are cold: 3. Salzbrun, Obersalzbrun, near Freiburg in Silesia; about 0.2 % sod. bicarb. 4. Bilin, in the vicinity of Teplitz. 5. Pachingen, and 6, Gielnau in Lahnthal, the waters of which are principally exported; also 7, Gieshubel, in the vicinity of Karlsbad. Bilin and Pachingen are quite rich in sod. bicarb., about 0.4 %; Geilnau and Gieshubel with about 0.1 %. And very recently Apollinaris springs (Ahrthal) are recommended.

To class b, the alkaline muriatic mineral waters, belong the following springs, which are considered the most important of this group:

1. Ems in Lahnthal, the most celebrated, if not the strongest sodium spring. Several springs that differ rather in temperature than in composition; the latter contain about 0.2 % of sodium bicarb., carbonic acid, and perhaps 0.1 of kitchen salt. The oldest of these are Kesselbrunnen (46°C), Krachuchen (35C°), lately Wilhelmsquelle (49°C), Victoriaquelle (27°C), Augustaquelle (39°C). 2. Luhatschowitz in Machrar, one of the strongest soda springs (about 1.0 %), and rich in sodium chloride. 3. Selters on the Tuunus, the waters of which are only exported, contains almost 0.2 % sod. bicarb, and about 0.3 % sod. chloride. 4. Gleichenberg in Steyermark, about the same composition as that of Ems, but it is cold.

POTASSIUM CARBONATE AND BICARBONATE.

The neutral potassium carbonate—potassium carbonate (K_2CO_3) is obtained from the ashes of wood by lixiviation with water. The solutions are evaporated, and the residue calcined. The product is the crude potash (potassium carbonicum crudum), a grayish white, for the most part soluble, very deliquescent, and acrid tasting powder.

By continued purification potassium carbonicum depur is obtained, a white, dry, easily soluble powder, containing about 95 % of potassium carbonate.

By exposing the acid potassium tartrate to a red heat, we obtain the almost pure potassium carbonicum purum.

The sodium bicarbonicum—hydrogen and potassium carbonate—$KHCO_3$, prepared by passing a stream of carbonic acid gas through a solution of the foregoing salt; colorless and permanent crystals are formed, soluble in water and alcohol.

Physiological action.—In describing the physiological effect of these salts when taken inro the animal body, upon the individual organs, we should have to repeat almost word for word what has been said concerning sodium carbonate; for the toxic effect of potassium, when introduced by the stomach, need not be taken into consideration.

However the potassium carbonate is borne with greater difficulty by the stomach, and more easily produces gastric catarrh, especially after long continued use, for which reason the sodium carbonate is in most cases preferable, with the exception of cases in which we desire a diuretic effect, when potassium would be desirable, its diuretic action being considered stronger; or in gout, because of the greater solubility of the potassium urates as compared with the corresponding sodium salts.

Therapeutic Application.—This will be treated of (on page 42) together with sodium carbonate, etc.

Dosage and Preparations.—Internally, the preparations of the potassium carbonate are used chiefly in the form of "saturationes" (see page 38.) Externally, however, potash is more used than soda. Dosage like that of the sodium salt.

1. Potassium carbonicum crudum—Cineres Clavellati, potash of commerce.
2. Potassium c. depuratum (obtained from the "Cineres Clavellati.")
3. Potassium c. purum (obtained from "Tartaro").
4. Liquor potassii carbonici—contains 33 ⅓ % of potassium carbonate—0.5–2.0 (5–30 drops).
5. Potassium bicarbonicum.

As to the other preparations, compare with sodium carbonate and bicarbonate.

LITHIUM CARBONATE.

The carbonate of lithium, the only salt of lithium which has as yet been used, is a white, odorless powder, of a strongly alkaline taste.

Inasmuch as lithium is only slightly soluble in water (rather more soluble in water impregnated with carbonic acid) it may be considered as the mean between the metals of the alkalies on the one hand and the alkaline earths on the other.

Physiological Action.—When administered in therapeutic doses, by the stomach, there is no more danger of an injurious effect upon the heart, from this salt, than from the potassium salts. Its taste is disagreeably alkaline. When introduced into the stomach it is easily absorbed, and can be traced, according to Bence Jones, by means of its spectrum, in all the tissues. It is said to be strongly diuretic, more so than the potassium salts. By some it is supposed to increase the excretion of urine, others believe it diminished under its influence.

It is said to possess a greater solubility for uric acid than the corresponding potassium salts. According to Lipowitz and Ure, 250 parts of a solution of a lithium carbonate, at a temperature of 38° will dissolve almost 1,000 parts of uric acid. According to Garrod, if pieces of cartilage and bones of gouty patients, which are incrusted with sodium urate, be placed in solutions of lithium, sodium and potassium of equal strength, we will find after a certain time that the portions lying in lithium solution will be freed of the urate, while those placed in the potassium and sodium solutions will be unaffected

Therapeutic Application.—Since Garrod's observations lithium is used in gout. This observer found that the gouty deposits were diminished and finally disappeared. In many cases the frequency of the attacks were diminished and the constitution of the patient improved. Since then it is greatly preferred to the preparations of potassium and sodium. Whether indeed lithium is practically of more utility in gout our experience has not yet determined, although theory is in favor of this view. However, the indications and counter-indications for the use of lithium preparations in gout are the same as those for the use of the sodium and potassium salts. The same may be said of its use in gravel. From being used in true gout, it has come to be applied to arthritis deformans, and furthermore to rheumatism. As to its utility in these affections, experience has not yet demonstrated it. The recent recommendation that carbonate of lithium should be used as an inhalation in croup and diphtheria is probably only of temporary signification.

Dosage.—0.005–0.3 per dose (1.5 per day) in powder or carbonic acid water. Struve's carbonate of lithium water contains 1.0–1000.0, 1–3 liters to be taken daily. Several natural mineral waters contain lithium, as for example: Durkheim, Salzschlirf, and Baden-Baden.

3.—THE ALKALIES WITH THE VEGETABLE ACIDS.

PHYSIOLOGICAL ACTION.

The tartrates, acetates and citrates of the alkalies are partly altered in the intestine into bicarbonates and appear in the urine as carbonates. According to Buchheim, this change is partly owing to a fermentative process and partly to the action of the carbonic acid present in the intestinal canal, in consequence of which the liberated organic acids are absorbed into the blood, while the bases remains in the intestine as bicarbonates. (Compare with this pp. 9 and 10.)

Inasmuch as experiments made with the salts of the alkalies and vegetable acids, have shown that their physiological action is exactly similar to that of the carbonate, there is no reason why we should repeat what has already been said, and we would refer to what has been said when speaking of the carbonates.

It is quite uncertain whether the acetates have a greater diuretic effect than the carbonates; at least we could not confirm a difference when making use of both salts. There are no exact observations upon this point; but since even when the acetates of the alkalies are introduced, they come to exist in the blood of the kidneys as alkaline carbonates, there scarcely seems any reason for the assumption that they have a stronger diuretic effect.

The cathartic effect, like that of the carbonates, is very uncertain.

We do not hesitate, therefore, to express the belief that the salts with the vegetable acids are entirely unnecessary in practice, being sufficiently well represented by the carbonates.

POTASSIUM ACETATE—POTASSIUM ACETICUM.

The potassium acetate ($C_2H_3KO_2$) is a very deliquescent, almost neutral or only slightly alkaline salt; readily soluble in water and alcohol.

Therapeutic Application, compare page 42.

To be given in doses of 0.5–3.0 (10.0 per day) in solution, but generally given in form of "saturation"; sometimes also as a pill together with other active substances. (*e.g.*, radix rhei.)

1. *Liquor potasii acetici*—clear, colorless and containing 33⅓ % of potass. acetat.; in doses 2.0—10.0 (50.0 per day).

SODIUM ACETATE—SODIUM ACETICUM.

The sodium acetate ($C_2H_3NaO_2+3H_2O$) is deliquescent like the potassium acetate, and can be administered as a powder.
Like potassium aceticum—superfluous. Same dosage.

NEUTRAL AND ACID POTASSIUM TARTRATE. POTASSIUM TARTARICUM ET BITARTARICUM.

The neutral potassium tartrate $\left.\begin{matrix}K\\K\end{matrix}\right\} C_4H_4O_6$ forms transparent crystals of a salty bitter taste, and is very easily soluble.
The acid potassium tartrate $\left.\begin{matrix}H\\K\end{matrix}\right\} C_4H_4O_6$ has an acid taste and dissolves with difficulty (1:180 cold, 1:20 hot water).

THERAPEUTIC APPLICATION.

Dosage 1. Pot. tart. in small doses; 0.5–2.0 (8.0 per day) as a laxative 15–40.0 per dose.
2. Pot. bitartaricum—cream of tartar—Tartarus depuratus—"argol" in doses of 0.5–3.0 (10.0 per day); as a cathartic, 2.0–8.0 in powder (soluble with difficulty).
3. Sodium tartaricum—sodium tartrate—has little taste—readily soluble; this salt is entirely superfluous.

POTASSIUM AND SODIUM TATRATE—TARTARUS NATRONATUS.

The tartarte of soda and potash or Rochelle salt $\left.\begin{matrix}Na\\K\end{matrix}\right\} C_4H_4O_6+4H_2O$ forms large, transparent, rhombic prisms, is readily soluble in ½ part of cold water, and has a saline bitter taste.
Application and dosage like that of cream of tartar. Entirely superfluous.

THERAPEUTIC APPLICATION OF THE ALKALINE CARBONATES AND ALKALINE COMBINATIONS WITH VEGETABLE ACIDS.

There is as great a similarity in the therapeutic action of the carbonic and vegetable acid salts of potassium and sodium as there is in the physiological action. It is generally only empirically or perhaps by a sort of preference, that we select one of these salts for any particular purpose rather than another. In general the same indications hold good for all of these preparations, and we therefore consider it best, in order to avoid repetition, to give the indications both for the carbonic and vegetable acid salts together, particularizing, however, in each particular case the preparation most commonly used.

These salts are principally indicated and best emyloyed in chronic catarrhal conditions of various mucous membranes.

They are also used in chronic catarrhal gastritis, and also in several other diseased conditions of the mucous membrane of the stomach and in digestive disturbances. For this purpose the best

results will be obtained, if, the diet having been regulated, they are administered in the form of alkaline mineral waters in which they exist generally in combination with other salts. When prescribed as a medicine, the sodium carbonate is the salt administered almost without exception. Sometimes the potassium acetate is used in the form of a saturation and lately this has been even generally recommended. Not much, however, is to be expected from its use, and we believe its only indication to be ut aliquid fiat in an acute febrile morbus fiens. Under the following conditions the alkalies are used with some prospect of success. First of all in chronic gastric catarrh. It is well known that in any individual case it is not always easy to decide whether a chronic dyspepsia or other symptoms pointing to a disturbance of the functions of the stomach is the result of the morbid anatomical changes of an actual catarrh. If this be really the case, however, then the alkalies combined with a suitable diet are the best remedial agents. The methods of administration are various. Either the alkali is simply ordered from the druggist in powder, or solution, or in the shape of troches (of Vichy, Ems or Bilin). Another method is to wash out the stomach with sodium bicarbonate, a procedure which lately is quite often resorted to even in ordinary gastric catarrh, and one which we can recommend from personal experience. And finally a method, which, if practicable, is the best, namely the systematic use of the alkaline mineral waters; either the simple ones, or preferably those containing in addition to the alkaline carbonate and free carbonic acid, a larger or smaller amount of sodium chloride and very often even those springs are used which, in addition, contain sodium sulphate (compare with chap. on this salt), and this without the presence of prominent symptoms referable to the intestine. Again, the alkalies administered in one of the above-mentioned ways often have an admirable effect upon the complex symptoms which characterize the condition known as status gastricus, loss of appetite, an abnormal taste in the mouth, nausea, sometimes even vomiting, belching of gas, a feeling of pressure and fullness over the stomach, a more or less coated tongue—a dyspeptic condition so often seen either as an accompaniment of acute or chronic maladies (as for instance in phthisis) or as an independent condition, especially frequent in those who live well and take little exercise. Whether this is really dependent upon a catarrhal condition of the mucous membrane of the stomach has not yet been shown. (*Traube.*) We should, however, state that in this condition

on page 36. Experience has shown that they are of greatest utility in those catarrhs in which the secretion of mucus is very slight, while they have little or no effect in bronchorrhœa. We must take into consideration, however, in estimating their value when taken directly at the springs, the influence of the change of air, etc.; whether they are of radical utility in the frequent follicular catarrh of the pharynx we have never been able to determine, but as adjuvants to other therapeutic means they are incomparable. We must emphasize the fact that the catarrh of the respiratory tract must be a simple idiopathic one, for the use of mineral waters, of which Ems and Salzbrun are the most popular, rarely affects the primary disease which is at the basis of the secondary catarrh. Both of these springs must be avoided, as experience has shown us, in cases of phthisis, especially if there be a tendency to hæmoptysis. And this is especially true of Ems, to which notwithstanding even to-day patients with phthisis and hæmoptysis are sent. Although invaluable in the ordinary chronic catarrhs, with or without emphysema, yet it can easily do much harm where a tendency to hæmoptysis exists, both on account of the carbonic acid that it contains and the temperature of the water if taken at the springs.

Whether the great reputation which the local application of the alkaline waters, especially Ems, enjoys in the treatment of *chronic metritis* and *catarrh* of *the vagina* is due principally or even in part to the effect of the alkali, is not positively determined. On the other hand, the most valuable remedy against chronic cystitis is found in the alkaline carbonate mineral waters (in which sodium chloride and carbonic acid are also constituents) without considering as to what may be the basis of this good effect. We need scarcely call attention to the precaution, however, that the symptoms of simple alkaline fermentation of the urine must not be mistaken for those of catarrhal cystitis in making out the therapeutic indications. Here we should prefer Ems, Vichy, Wildungen and Karlsbad.

Another application of the alkaline carbonates and salts of the vegetable acids which is based upon the theoretical physiological action and upon practical experience, is in lithiasis, *and where a tendency to* the deposit of sediments in the urine exists. Of course this does not apply to deposits of earthy phosphates. As to whether these salts shall or shall not be given in cases in which oxalates appear in the urine is uncertain; some observers considering the carbonate to be injurious on account of theoretical considerations, others believing it to be one of the

best remedies to cause the disappearance of the lime oxalate from the urine. On the other hand, these salts (carbonates and vegetable acid compounds of the alkalies) are of great utility, especially if combined with a proper diet in the so-called uric acid diathesis; their continuous use is followed by a diminution in the amount of uric acid in the urine, and a lessened tendency to the formation of concretions. That concretions already formed have become smaller and finally entirely dissolved has been repeatedly confirmed. The question as to whether this action of the alkalies upon the uric acid diathesis and the formation of concretions is only a symptomatic one or whether they act upon the cause of the condition itself has not yet been decided. The best method of employing these is again in the form of the water from the different mineral springs, and of these we should prefer, in cases of gravel, either Vichy, Karlsbad or Bilin. When the alkalies are to be prescribed, however, under their own form, then the sodium salts should be preferred in all of these cases, because their long continued use is not so easily followed by digestive disturbances. It is true that some physicians, and especially English ones, prefer the potassium salts in the uric acid diathesis for the reason that the acid potassium urate is slightly more soluble than the similar sodium salt. This slight advantage, however, does not compensate for the increased digestive disturbances caused by the potash salt. The utility of these salts in gout (arthritis urica) is, according to the decision of the best observers, beyond question, and here the potassium preparations are preferred to those of sodium; first, as has just been stated, on account of their slightly better solubility; and secondly, because the potassium salts are at the same time more strongly diuretic. Experience has shown them to be of utility in the treatment of an acute attack of gout, but decidedly more useful is their continued use in the so-called chronic gout at a time when there is no acute inflammation present in the joint, and furthermore in the treatment of the gouty diathesis and the removal of gouty deposits. We sometimes see under the influence of this treatment patients, who for years have suffered from severe and numerous attacks of gout, remain free from them for a long time, and their general health improve (Garrod). This treatment is contraindicated, however, in very old individuals or when a serious kidney complication exists. In chronic cases the most practicable is the use of *one of the mineral* waters (Vichy, Karlsbad, Neuenahr; or *Marienbad, Wiesbaden*, Homburg and Baden-Baden.) When

prescribed, the salt should be administered in small doses, frequently repeated, and in very dilute solution upon an empty stomach, a short time before meals. In chronic digestive disturbances with the gouty diathesis, the sodium carbonate should be preferred. Massyer, who had discovered uric acid in the gouty concretions even before Garrod, and considered it as the cause of the gout, was accustomed to use the potassium acetate.

The alkaline salts, with carbonic and vegetable acids, are much used as diuretic agents, and of these the most popular is the potassium acetate; and we must therefore believe this salt to be the most diuretic. The indications are the same as those given for the use of potassium nitrate. P. Frank, Bright and others were especially fond of the potassium bitartrate, but its diuretic effect is probably not greater than that of the other salts.

In *diabetes mellitus* the alkaline carbonates have been largely used since the time of Mialhe, whose theory of diabetes was such as to almost necessitate the use of this remedy. The theory is disproved, but experience has not shown the futility of the treatment, especially if it be administered in a certain manner. It is true that most observers have had very little result from the pharmaceutical use of these compounds, and even the few favorable reports (Greisinger, Pavy,) speak only of an improvement in the general health and the subjective symptoms, and not of a diminution in the quantity of the sugar. On the contrary, in advanced cases, as in those of consumption, the alkaline carbonates are more likely to do harm; and even in the earlier stages they may be injurious by the disturbances produced in the digestive functions when continued for too long a time and in too large doses.

But it can not be denied that large numbers of observations have proved that the use of some, not all, of the mineral waters containing alkaline carbonates has had a good effect upon diabetes. These are Karlsbad, Neuenahr and Vichy. It is questionable, however, whether the alkaline carbonates contained in these springs are the cause of their good effect, especially when the uselessness of their pharmaceutical administration, and of other waters equally rich in these salts, be taken into consideration (Senator). However, we are decidedly of the opinion that notwithstanding the lack of any theoretical explanation for its action, daily experience has undoubtedly *proved the great utility* of Karlsbad in this affection. At present *it is generally* agreed, however, that even the use of the

above-mentioned waters does not cure the diabetes, but they diminish the intensity of the worst symptoms, in many of the cases, and cause the disappearance of sugar from the urine for a greater or less period, while the patient is under treatment, and this even while a certain amount of carbo-hydrates are given with the food, and thus life is prolonged. The etiology of the diabetes offers no indication for the use of the mineral waters; diabetes of neural origin is as easily improved as the other forms. That there are indeed any contra-indications to the use of the Karlsbad waters is on the one hand disputed (by Seegen), on the other affirmed. J. Mayer considers it contra-indicated when serious complications exist (such as gangrene of the skin, phthisis, coarse cerebral lesions, albuminuria with excessive anæmia, considerable weakness of the heart, etc.), while Seegen saw an improvement take place in the diabetic symptoms even with extensive tuberculosis.

In *acute poisoning with* the acids, the alkaline carbonates are efficient antidotes, although not superior to chalk and magnesia.

These, then, are the conditions in which experience has shown that the salts of the alkalies with carbonic and vegetable acids are of greater or less utility. We shall add the following remarks, however, for the sake of completeness:

In excessive deposition of fat the alkaline carbonates are entirely without effect. In officinal form they are never administered, and the favorable effect of Karlsbad, Marienbad, etc., should be ascribed to the alkaline sulphates and their cathartic action. The potassium tartrates are still used by some physicians as cathartics. But since there is no reason why these should be preferred to other saline cathartics, even in abdominal plethora, hæmorrhoids, etc., and since we already have a sufficient number of the latter, we consider it best, in spite of their "useful effect," to drop them from our practice, and thus lighten our overburdened materia medica. All of the so-called "cooling effect" of cream of tartar in febrile diseases is nonsense. All the other conditions in which the salts of the carbonic and vegetable acids, with the alkalies, are used or were used, we shall not even mention by name, not even excepting the much-vaunted utility of these salts in acute articular rheumatism, which we must declare as entirely without foundation. Of all of these salts potassium carbonate alone is used externally, and, as might be expected, recommended for a large number of conditions. But in most cases the alkaline carbonates are with advantage replaced by other preparations and

methods of treatment. Solutions of potash seem to be of a certain amount of utility in pityriasis simplex, pityriasis versicolor, and ichthyosis and as irritating local washes.

4.—THE ALKALINE PHOSPHATES.

PHYSIOLOGICAL IMPORTANCE.

The function of the alkaline phosphates in the blood and tissues is not yet thoroughly understood. The views held concerning this point, as well as the form under which they exist in the organism, having undergone many changes in the last few years, especially through the researches of Maly.

While it was formerly believed, that in the tissues there existed only acid phosphates, while in the blood serum only basic alkalies or neutral alkaline phosphates were contained, Maly proved that—

1. Blood serum, in spite of its general alkaline reaction, contains acid reacting salts; the occurrence of the acid sodium phosphate (monosodicphosphate NaH_2PO_4) is perhaps the most easily understood. For, as Berzlius, and after him Setschenow, proved that the carbonic acid and the so-called neutral sodium phosphate (bisodicphosphate Na_2HPO_4) are changed into the monosodicphosphate (NaH_2PO_4), and sodium bicarbonate (NaH_2CO_3), when brought in contact with each other. But in the blood we have also free carbonic acid present, the result of which is that there must also be present a certain quantity of acid reacting sodium phosphate. This acid phosphate can maintain its integrity even in the presence of these alkaline salts (bisodic phosphate and sodic bicarbonate)—the reaction of the former is overpowered by that of the latter. Both phosphates present a picture, so rare in chemistry, of two bodies of opposite reactions which do not react upon one another, although one is acid and the other alkaline.

2. Even the alkaline substances contained in the blood (bisodic phosphate and sodic bicarbonate are theoretically acid bodies, although they are reckoned among the alkaline bodies because they turn litmus blue. But according to their chemical constitution they are not basic but acid salts. For they can both unite with another atom of hydrogen which could be replaced by a metal, as in the hydroxyl group.

$CO\begin{cases} OH \\ ONa \end{cases} : \quad PO\begin{cases} OH \\ ONa \\ ONa \end{cases}$ and by means of this hydroxyl (HO); they are able to imitate acids and combine with bases.

3. The distribution and mutual combinations of these acids (phosphoric and carbonic) and bases in the blood is highly complicated, and at present not entirely understood. Analysis of the ash residue is of no utility for the study of these combinations, for nothing would be more fallacious than to attempt to group the oxides and acids as thus obtained. We can only know that in the blood serum acids and bases are distributed in many combinations, and among these numerous neutral, and because of the presence of free carbonic acid, numerous acid compounds must be found existing at the same time and together; finally, that alkaline substances, as such, only exist in the blood in an empirical sense—that is to say, in so far as they turn litmus blue.

4. As Graham has shown, the acids and acid bodies contained in mixture of basic, neutral and acid fluids diffuse out more rapidly than do the basic and neutral substances; the difference between the diffused (acid) portion and the original fluid is greater, the more perfect the diffusion apparatus. In this way can be explained much more easily than could be by the old hypotheses, how it is that acid fluids (gastric juice, acid urine) can be secreted from an evidently alkaline blood. The origin of free hydrochloric acid in the gastric follicles, which is diffused from the blood into the stomach, is explained by the occurrence of acid and neutral sodic phosphate in the blood, both of which salts are able, in combination with the chlorine of the blood (*e. g.* sodium chloride, calcium chloride), to form hydrochloric acid, which, from its greater diffusibility, easily diffuses. The origin of the acid in the urine of carnivorous animals and men is similar to that of that of the gastric juice. The occurrence of the acid—alkaline phosphate in the urine is easily explained. For the carbonic acid, as well as the other acids which are the result of tissue metamorphosis, namely, the uric and hippuric acids, etc., change the neutral bisodic phosphate of the blood serum into the acid salt, which is easily separated while passing through the fine capillary system of the kidney.

5. From what has been said it will be seen that the blood possesses an inherent power of regulating and maintaining its reaction and normal percentage of alkali, inasmuch as only acids and acid salts are excreted with the urine; this is further shown by the fact that the urine of men and dogs becomes alkaline during the digestive process, because at this *time another* and more perfect dialysing apparatus, namely *the glandular* apparatus of the stomach, is separating a

large quantity of acid from the blood before it reaches the kidneys.

6. The blood of the herbivora is poorer in phosphoric acid and richer in alkali than that of the carnivora: as a result we have a constant alkalinity of the urine in herbivora.

The phosphoric acid salts have not only an important part to play in the blood, and the formation of the acid excretions, but also in the construction of the tissues; for they are found in all the tissues, not only in the carnivora but also in the herbivora in large quantities, although the food and blood of the latter contain only small quantities; the phosphates also exist in larger quantities in cells, which later on become rich in alkaline carbonates.

SOIDUM PHOSPHATE.

The sodium phosphate, bisodic-phosphate ($Na_2HPO_4+12H_2O$) crystallizes in large, colorless, transparent, rhombic crystals, which rapidly effloresce in dry air, without however breaking up, and which when calcined are changed to the sodium pyrophosphate. Its reaction is neutral. It has a cool, salty, and not unpleasant taste, is very readily soluble in 2 parts of warm and 6 parts of cold water.

PHYSIOLOGICAL ACTION.

According to Ludwig, dilute solutions of this salt, which by chance is independently used in therapeutics, have a property similar to that of dilute solutions of sodium chloride, that is, they preserve the irritability of nervous tissue placed in them, for a long time. When internally administered in larger doses it diminishes all the excretory functions of the body, diminishing even the amount of sodium chloride excreted (Boecker). Its cathartic action is positively determined and acts in the same manner as the sodium sulphate. But on account of the large amount of water which it contains it must be given in large quantities in order to attain this effect.

According to Rutherford the amount of bile secreted is greatly increased by the salt: (for every hour, and for every kilogram in the weight of the dog, there is an increase from 2.1 to 3.7 grms). The bile becomes more watery, the mucous membrane of the small intestine injected, with, however, no increase in the secretion.

Larger quantities (10.0 grms.) injected into the blood are said *to produce a tetanoid* condition, followed by death with gen-*al paralytic* symptoms (Falck.)

THERAPEUTIC APPLICATION.

The medicinal application of sod. phos. is no way what would be expected from its physiological action.

For theoretical reasons it has been tried in a large number of conditions, (Osteomalacia, Rachitis, Scrofulosis, etc.,) without experience having shown any evident benefit. It has also been recommended in the uric acid diathesis, but has no advantage over the alkaline carbonates, which are so easily administered in the form of mineral waters. Lately it has been recommended in small doses by Stephenson for the diarrhœa of children, especially such as receive no breast milk, or have been weaned; but here, also, extensive experience is still lacking. Its only well founded use is as a cathartic; and here it is only distinguished from other saline cathartics by the more agreeable taste and higher price.

Preparations and dosage—1—Sodium phosphate 0.5–2.0 in powder and solution—as a laxative, 15.0—30.0; for children, 0.1—0.5, with the food.

2—Sodium pyrophosphate—entirely superfluous—application and dosage same as foregoing salt.

5. THE ALKALINE SULPHATES.

PHYSIOLOGICAL IMPORTANCE.

The potassium and sodium sulphate are normal ingredients of the body, into which they are partly introduced as such with the food, and partly formed in the body by the oxidation of the sulphur contained in the albuminoid bodies, into sulphuric acid, which combines with one of the alkalies which are present. It is then excreted, principally by the urine, in larger quantities during animal diet and in smaller quantities during a vegetable diet, and is doubtless a product of the regressive tissue metamorphosis, and is to be excreted from the system (Goup, Lehman). Its excretion, therefore, takes place under similar circumstances as that of the urea.

In the intestines a portion of the salt is reduced to metallic sulphides.

For us the action of the medicinal alkaline sulphates upon the intestine is of the greatest importance.

Sodium Sulphate—Glauber's Salts.—The neutral sodium sulphate—Sodium sulphas, ($NA_2SO_4+10H_2O$) forms large transparent crystals, which *slowly effloresce in the air*, water being given off, and a white powder left; is *easily soluble (in 1-3 part* of water at 33°) and has a salty bitter taste.

PHYSIOLOGICAL ACTION.

Digestive Canal.—Small quantities (0.5 grms.) taken once have no effect. Even when taken oftener, at 5-hour intervals, there is no effect; taken every hour, however, after a time the same cathartic effect is produced as after a large dose.

Larger quantities (15.0—30 grms.)produce a large amount of gas (partly sulphuretted hydrogen), rumbling in the intestines, discharge of ill smelling flatus, and after several hours dark, watery stools, which are repeated several times. Even after 24 hours the fæces are still softer than normal. The concentration of the solution is of little importance, for the laxative doses given above produce their effect whether given dissolved in 100 or 1000 grms. of water.

Generally the appetite and stomach digestion are unaffected, only exceptionally nausea and vomiting occur, and then probably as a reflex result of the irritation of the organ of taste.

Tormina are rare, and if they do occur they are very slight. When continued for too long a time, the appetite begins to fail and as a result of the constant diarrhœa we have wasting of the body, or at least a decrease in the quantity of fat and bodily weight. The *biliary secretion* is very much increased, so that experiment confirms the results of the clinical experience obtained at Karlsbad. It is remarkable that the Epsom salts show none of this cholagogue action (Rutherford).

Urinary Excretion and Transformation of Nitrogenous Materials.—Small doses, which are slightly or not at all cathartic, do not affect the amount of urine excreted to any marked degree. We have, however, several observations of which some show an increase and some a diminution in the amount of urine. The sulphuric acid of the urine, however, is increased, and that most of all when this salt is given in oft-repeated small doses. Yet, on the whole, the urine is said to become less acid, and after long continued use even alkaline (Woehler, Mialhe.)

Seegen reports, that upon the introduction of small amounts of Glauber's salt (2.0 grms.)the nitrogen passed out from the body has been very much diminished, even as much as 24 per cent. But Voit found, as a result of more accurate experiments upon dogs, that during the administration of the salt, only the amount of water absorbed and relatively the amount of urine excreted were increased, while the relation between the amount of nitrogen introduced and the amount excreted remained unaltered; that therefore this salt has no influence upon the metamorphosis of the albuminoids in the body.

The theory of the cathartic action has already been discussed in a separate chapter* in the introduction.

THERAPEUTIC APPLICATION.

What we are about to say, applies to the various saline cathartics, not only to the alkaline sulphates; as we have several times remarked, we could easily do without the large majority of them ; they are entirely unnecessary. The magnesium sulphate and the corresponding sodium salt, together with the many mineral waters that contain these salts as active ingredients, are sufficient for all purposes and cases occurring in practice.

We can not here attempt to analyze the various cases in which cathartics are indicated, but must limit ourselves to a specification of the particular circumstances in which the salines should be preferred to the other cathartics, or where, at least, they are not contra-indicated.

In chronic constipation, the salines are sometimes properly preferred, and that under the form of some mineral water, which, if possible, should be taken at the spring, because in this way the dietetic rules that have been laid down are most likely to be carried out by the patient. We must, however, take the etiological conditions of the individual cases into consideration, for not all cases of chronic constipation are properly treated by salines. They are most indicated, perhaps, in cases of this kind occurring in people who lead a sedentary life and live well. In the absence of the latter indication, we should always first try regulation of the diet. Sometimes these salts have an excellent effect in constipation, due to chronic catarrh of the small intestines ; although when slow peristalsis of the large intestine is the cause, the good effect is not so decided. Here we would speak of the use of the saline cathartics in excessive fat deposits, excellent results are often obtained by a combination of a properly selected mineral water and a fitting diet. In the choice of a spring, we should be guided by the circumstances of individual cases, whether of abnormal fat deposit, or chronic constipation ; in strong powerful persons, with a healthy color to the skin and firm muscles, Marienbad and Karlsbad have a good effect ; if, however, the muscles are flabby and ill developed, skin pale, then Franzensbad or Elster should be used. The various springs in Tarasp are good for both sets of cases. (Compare in this connection, the *sodium chloride* springs).

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*See pages 29 and 31.

Glauber's salts and the salines in general are furthermore administered, when we wish to withdraw water from the organism through the intestine. This is especially the case in dropsy, when the amount of water excreted by the kidneys is very small in amount, or when it is desirable to increase it.

Thus in dropsy due to heart disease, emphysema of the lungs, chronic nephritis, etc.

Furthermore, on this principle we give salines in acute inflammatory febrile affections, especially of the serous membranes, as soon as a cathartic effect is admissible. We can not readily see why these cathartics should here be preferred to others; nor does experience indicate any reason. Even in the later stages of inflammations of the serous membranes with exudations, it is very questionable whether the watery stools have any influence upon the re-absorption of the exudation. In cerebral hyperæmia the saline cathartics have certainly a good effect by the amount of water which they abstract, but that these are in any way preferable to senna, is a matter which we have not been able to confirm. For these reasons these salts may be given in inflammatory affections, without being considered as superior to other cathartics or deserving of preference to these.

The use of the cathartic salts presupposes that no inflammatory or ulcerative condition of the stomach or intestines exists; should this be the case, that is to say, should in the course of ilio-typhus, dysentery, etc., a laxative be necessary, we must employ other cathartics (ol. ricini, calomel) or clysters. The contra-indication which has always been insisted upon, namely inflammatory affections of the urinary apparatus, is not of great importance, inasmuch as physiological researches have shown that when the salines are given in large doses and a purging is the result, little of the drug is absorbed. Experience also teaches that even in acute nephritis, Epsom and Glauber's salt can be administered without harm. As the general result of experience in the use of these *salts as ordinary purgatives* we would say, that they are better borne by persons of strong constitutions with a well developed muscular power, than by weak, deteriorated individuals.

The sodium sulphate, in particular, has been lately recommended by Ziemssen for the treatment of *ulcer of the stomach;* a recommendation which has been repeatedly confirmed and to the utility of which we also can bear witness. Ziemssen believes that the principal factor in the healing of ulcer of the stomach, is the separation as quickly as possible of the acid

peptones from the stomach. This effect will follow if the peristaltic movement of the intestines be hastened; and this can be best accomplished by the sodium sulphate administered in the form of artificial Karlsbad salt, which is almost entirely composed of Glauber salts and only contains small traces of sodium chloride and sodium carbonate. The patient should take, every morning upon an empty stomach, on an average 1–2 teaspoonfuls of the salt, in ½ liter of boiled water, cooled down to 44° (R).

Dosage and Preparations.—1. Sodium sulphuricum depuratum. Sal. mirabile Glauberi—Glauber salts:—as a laxative from 15.0–50.0 at a dose or in two doses with an intermission of one hour between them; can either be given in solution or as a confection.

2. Sod. sulph. siccum contains no water of crytallization—as a laxative from 5.0–25.0.

3. Alkaline and saline mineral waters — sodium springs containing Glauber's salts.—The springs of this class contain sodium sulph. in larger or smaller quantities as their principal active ingredient, in addition to considerable, or, perhaps, equal quantities of sodium carbonate, sodium chloride and carbonic acid. It is supposed that the presence of these substances make it possible to use the mineral water containing Glauber's salts for a long time without producing any digestive disturbances. It is true that in many springs the Glauber's salt occurs in conjunction with magnesium sulphate, but these will be considered under the head of Epsom salts.

The alkaline-saline mineral springs, because of several of their representatives, belong to the most important and best of the springs which we possess.

1. Karlsbad in Bohemia.—The numerous springs are distinguished rather by the various temperatures of the water, than by any variations in their active ingredients. They contain about 0.2 sodium sulphate against 0.1 of sodium chloride and 0.1 of sodium carbonate, carbonic acid and small amounts of other substances. The temperatures are as follows:—Sprudel, 74°C.; Schlossbrunnen, Mühlenbrunnen, Theresienbrunnen, Markbrunnen, between 51 and 56°C.; Bernhardsbrunnen, 69°C.

2. Marienbad in Bohemia: cold springs, (9°) contain double the amount of sodium sulphate found in Karlsbad (almost 0.5 %) and also a slight trace more of sodium chloride; on the other hand, less of sod. carb. The two most important springs are, Kreuzbrunnen and Ferdinandsbrunnen. 3. Tarasp in Lower Engedin should be here considered, with the Lucius and Emerita springs; both cold, about 7°C., and containing about a similar amount of sod. sulph. as Karlsbad, but three times as much of sod. carbonate and chloride and carbonic acid. 4. Franzensbad in Bohemia of about similar composition with Karlsbad but cold (10°); the traces of ferric carbonate contained in these springs, namely, the Saltz and Franzens springs, are so minute that they need not be considered, especially in the effect of large cathartic doses. 5. Elster in Saxony, very much like Franzensbad, also cold, but containing more ferric carb. 6. Rohitsch in Steiermark contains some sod. sulph. and bicarbonate, but very little of sod. chloride. *With the Glauber salt* springs are included the following which contain very *little of this salt;* that is, 7—Fuered in Hungary and 8, Bertrich in Eifel.

6. CHLORINE COMPOUNDS OF THE ALKALIES.

SODIUM CHLORIDE—CHLORINATED SODIUM—KITCHEN SALT.

Sodium chloride or chlorinated sodium ($NaCl$.) is a salt which is widely distributed in nature, being found in mines as rock salt, dissolved in the water of the sea (2.5 %) and in salt springs up to 25 %.

It crystallizes in colorless transparent cubes, melts at a red heat, is neutral in reaction, dissolves in less than 3 parts by weight of water is not much more soluble in hot than in cold water. Completely saturated solution contains 27 % salt—scarcely soluble in alcohol, insoluble in absolute alcohol.

PHYSIOLOGICAL ACTION AND IMPORTANCE.

Facts in General.—Kitchen salt is a constant and necessary component of the animal body and is present in all the fluids and tissues, probably in part at least as a simple solution. The blood of herbivora and carnivora contains a larger amount of this one salt than of all the other salts taken together—in 100 parts of the entire saline element of the blood, we have 57 parts of kitchen salt. While it forms the principle saline ingredient of all animal fluids, being found in large quantities in the blood serum, lymph, pus and inflammatory exudation, there are only traces to be found in the organized cell; in the muscular cell, and in the blood corpuscles, the chlorine, although originating from the sodium chloride is united with the potassium. The fact, that both of these substances, which are chemically so familiar, are yet constantly found in different parts of the organism, never replacing each other, points to considerable and important difference in the function of sodium and potassium chloride. *

Influence upon the diffusion of fluids (*Hydrodiffusion*) *in the animal body. The permanence of the proportion of cooking salt in the blood.*—The chief function of the sodium chloride present in the blood is, as Liebig very beautifully demonstrated, dependent upon the purely physical property of all salt solutions, of exerting a suction force upon all fluids, which are separated from them only by a membrane, and which have a smaller proportion of, or are entirely free from, salt. If in a vessel of water we place a tube partly filled with a saline solution and firmly closed by an animal membrane, we shall find that after a short time, and, in opposition to the force of gravity, the fluid in the latter will increase in quantity and rise in the tube, while at the same time

* Compare pages 13 and 14.

it can be shown that the water in the outer vessel which has hitherto been free from salt, is always becoming more saline, so that a portion of the salt in the salt solution is passing in a direction opposed to that taken by the water passing from without through the animal membrane. This property is possessed by sodium chloride in common with the other salt. But since sodium chloride, as has been already stated, is the principal salt in the organism, therefore this physical phenomenon is chiefly due to its influence. Furthermore, this suction power of salt solutions is increased by rendering them alkaline, while the outer fluid is changed to an acid reaction ; so that we can see "that in the animal body we find all the conditions united together, to make of the vascular system with its salty alkaline blood a most perfect suction pump, which does its work without stop-cocks, valves and mechanical pressure" (Liebig). Upon this purely physical force depends the ready absorption of the digested acid chyle into the blood, which is further aided by the rapid flow of the latter through the vessels.

Upon this also depends the interchange of materials from the living cell, for the latter, as, for instance, the nerve cells, and the muscle cells, in the ordinary course of their existence came to contain an acid material, which, as a consequence, while circulating in the tissues of these cells passes over into the surrounding bloodvessels, this current must evidently be stronger, the larger the quantity of blood. And, since the products of combustion which are formed in the cell, are constantly carried away in this manner, the cell is constantly restored to its normal functional activity. While a muscle which has been deprived of blood has all its irritability exhausted after a short series of contractions, one that has the blood circulating through it will contract 40,000 times without then having exhausted its entire contractile power.

Upon this property, in part, depends the remarkable constancy of the proportion of the sodium chloride contained in the blood ; for this remains, with but slight variations, almost constantly the same, whether large or small quantities of the salt be introduced with the food into the stomach. For, when the quantity of salt contained in the stomach and intestines is increased, purely physical causes will cause its absorption into the blood to be diminished, until it entirely ceases and a watery diarrhœa sets in. In consequence of this insufficient water supply we naturally have the blood again becoming concentrated, the result being a diminution of its quantity, a decrease in the *blood pressure* and the amount of urine excreted ; so that in

this interchange we have a sufficient safeguard against too large a loss of water from the blood. If too much fresh water be taken, it will, indeed, be absorbed into the blood, but owing to the increased amount of fluid the tension of bloodvessels raises the blood pressure, and through this, the excretion of water from the blood, by means of the kidneys and sweat glands, is increased.

Chemical Relations in the Organism.—The fact, that even after the absolute withdrawal of cooking salt from the diet for weeks, the blood maintains its original possession of this salt for a long time and with wonderful persistency, even when, for example, a severe diuresis is produced by drinking large quantities of water, seems, to a certain extent, to prove that a portion of the sodium chloride exists in the blood in molecular combination with the albuminoids. But from the constancy of the percentage of this salt present in the blood, we may conclude that the sodium chloride while in the blood does not take an active part in the chemical tissue changes, but assumes rather in this connection an indifferent part. Nevertheless, the supposition, which has not yet been proved, that the hydrochloric acid of the gastric juice and the sodium of the biliary salts are derived from the sodium chloride seems to indicate some chemical transformation. As to the further possibility of a chemical change, namely, a reaction with potassium phosphate ; of this we shall speak later on.

Influence upon Nutrition.—In the introduction to the alkalies and alkaline earths we quoted from Forster's observations concerning the importance of the salt supply, and the detrimental effect of the want of salt upon the system. These prove that salts in general and also sodium cloride are indispensable for the maintainance of life.

Bunge asks the question whether the sodium chloride taken into the body with the organic material of the food really suffices for the maintainance of the normal amount of chlorine and sodium in the organism, or whether it is necessary to add to the food sodium chloride from the inorganic kingdom. In answer to this question, he instances the fact that the herbivora, both domesticated and wild, show a desire for kitchen salt, and that hunters have been long accustomed to take advantage of this taste, and allure animals by the establishment of "salt licks." It is said that animals have "licked out" large grottoes in the soft salt containing strata of the Altai region. This desire for salt has never been shown by the carnivora or the animals living upon prey. On the contrary, the latter

seem to evince a repugnance to salty food. Whence this difference? Chemical analysis shows that the daily amount of chlorine and sodium taken with the food is on an average the same for one kilogram of the herbivorous animals, or one kilogram of the carnivorous animals. (This statement, however, was afterwards retracted by Bunge; according to his later calculations, plants contain less sodium.) Why then should the herbivora need an additional quantity of salt?

Bunge thinks it due to the difference in the amount of potassium, which in the diet of the herbivora is two or four times as great as in the carnivora. According to his own calculations and those of others, 1 kilogram by weight of the herbivora absorbs:

	KO	NaO	Cl
When fed upon—Clover	0.357	0.022	0.043
" " " Beets and straw .	0.292	0.067	0.060
" " " Grass	0.335	0.093	0.073
" " " Vetch	0.552	0.110	0.059

and 1 kilogram by weight of the carnivora (cats):

When fed upon—Meat.	0.182	0.035	0.031
" " " Mice	0.143	0.074	0.065

The introduction of the potassium salts into the system causes the withdrawal of large amounts of chlorine and sodium. After a series of experiments made upon men, Bunge found that of 18.2 grms. of KO that were absorbed, 10.7 grms. passed through the organism and withdrew therefrom 5.1 grms. NaO and 3.4 grms. Cl. On the fifth day of the experiment the amount of sodium excreted was far greater than the equivalent of the amount of chlorine excreted; so that apart from the sodium chloride, there has been an additional amount of sodium abstracted from the system (5.6 grms. NaCl. and 2.1 grms. NaO.) We can not, therefore, doubt that this abstraction takes place by means of a chemical reaction between the potassium and sodium compounds. When a potassium salt whose electro negative component is not chlorine, but, for example, phosphoric acid,—that is to say, potassium phosphate,—is brought in contact in a solution with sodium chloride,an interchange of electro negative component of the two salts takes place, and potassium chloride, and sodium phosphate are formed. As soon as potassium phosphate is absorbed into the blood, a reaction takes place between it and the sodium chloride of the blood plasma, and *the potassium chloride and sodium phosphate thus formed are excreted by the* kidneys as superfluities, so that the normal

constitution of the blood may be maintained. Thus the absorption of potassium phosphate into the blood necessitates the withdrawal of the chlorine and sodium, and this loss is repeated by an additional amount of sodium chloride. In favor of this theory, also we have the experiments of Reinson on dogs, and Boecker and Reinson on human beings, which prove that the contrary is also true, namely, that with the increased absorption of sodium the quantity of potassium excreted is also increased.

Inasmuch as the chief diet of the lower classes (as for example potatoes*), contains a larger amount of potassium than sodium, it would appear for the above reasons that sodium chloride is a necessity for the poorer portion of the population at least, and not as Klein and Verson thought—simply a condiment which men have become so accustomed to that they can not do without it.

In opposition to these opinions of Bunge, Forster instances his own experiments and those of Kemmerich, which go to show that the human body has an extraordinary retentive power for sodium chloride ; so that even after weeks of a diet rich in potassium, combined with the entire withdrawal of sodium chloride from the food, the normal amounts of sodium and chlorine were found in the blood, although the excretion of chlorine had almost entirely ceased. Kemmerich who, as far as possible, deprived a dog of the sodium salts for seventeen days, giving, however, large amounts of potassium salts, found in the blood serum of the animal almost entirely, sodium salts, (96.39% of kitchen salt and 3.61% of potassium salt), while the urine drawn at the same time contained on the contrary enormous quantities of potassium salts (94.94%), and only 5.06 of sodium salts.

"It must also be said that not all herbivora evince this desire for cooking salt ; most of these animals on the contrary receive no sodium chloride in addition to their food during the whole of their life. Were the conclusions of Bunge justifiable, then the organs and secretions of these animals should no longer contain any sodium, which certainly is not the case."

Forster also denies that sodium chloride has been proved, by the experiments of Wundt and others, to be of as much importance to the animal's existence as it is generally held to be. "How would we explain the possibility of the existence of the *carnivora* in whose diet the amount of the sodium chloride is

* Compare table, page 16.

of the smallest (0.11%) quantity; if we suppose that the neglect to add salt to the diet is so deleterious to the system. What should we think of the well being and growth of children who only receive in 1 liter of mother's milk 0.26 grm. of sodium chloride" (Wildenstein).

In fact Bousingault made a series of comparative observations extending over a period of thirteen months upon six oxen, of which three were fed upon an ordinary diet, without salt, while three others were fed upon the same diet with the addition of a certain amount of sodium chloride. He found that the addition of sodium chloride to the food was without influence upon the quantity of the flesh or fat or milk excreted by the animal. But the animals that had received the additional amount of salt presented a better appearance, better growth of hair, smoother skin, and were more animated, the sexual functions being more active than those which had not received the extra amount of salt, and of which the hide was rough and tangled, the animals being dull and inexcitable. Upon this Liebig's comments are, that evidently the salt quickened the interchange of materials in the body, increasing the activity of the secretory functions and thus improving the general health of the animal. Even if the amount of flesh was not increased, yet the evil conditions which were present under the unnatural circumstances by which the animals were surrounded were neutralized by the administration of this salt. The long continued use of large quantities of sodium chloride (very salty food) in the diet has also been given as the cause of scurvy; there are no observations, however, upon which such a theory can be founded.

Influence upon tissue metamorphosis.—With the administration of sodium chloride we have a proportional increase in the amount of nitrogen separated in the body, together with an increase in the amount of urine excreted. First, because the thirst resulting from the administration of cooking salt increases the amount of water taken in, which alone would result in increased amount of nitrogenous metamorphosis; and further, because of the direct effect of the salt itself for the amount of urine excreted rises with the quantity of sodium chloride absorbed, even when no water is given, as will be seen from the following table:

Without an additional supply of water.

	Grms.	Grms.	Grms.	Grms.
Kitchen salt taken into the body	—000.	5.	10.	20.

Urine excreted	935	948	1042	1284
Urea	108.2	109.1	109.6	122.6

With an Additional Water Supply.

	Grm.	Grm.	Grm.	Grm.
Kitchen salt taken into the body,	0	5	10	20
Urine excreted,	828	898	987	1124
Urea,	106.6	110.0	112.2	113.0

Voit also considers that the increased transformation of the nitrogenous materials is due to the increased hydrodiffusion caused by the sodium chloride.

Excretion.—Sodium chloride is found in all of the secretions and excretions in considerable quantities, in the urine, sweat, mucus, tears, and fæces. It is most abundant in the urine; in which the average daily excretion of sodium chloride in men is 10–13 grms., that is 0.41–0.54 per hour. In women and children the amount is very much diminished, (in a woman 43 years of age, 5.5; in a girl 18 years old, 4.5; in a 16 year old boy, 5.3; in a 3-year-old boy, 0.8 grm.—Bischoff.) More is excreted about the middle of the day after dinner, least of all at night. An increased absorption of sodium chloride is followed by an increase in the amount secreted by all of the secretions. The amount is diminished during sleep and rest, and increased under the influence of hard work, great mental activity, and furthermore, when a large amount of water is drunk. The amount of urine and urea excreted varies directly and to a parallel extent with the diminution and increase of this salt.

In disease we find noteworthy alterations in the excretion of sodium chloride. In all febrile diseases (meningitis, pneumonia, and inflammation of the different serous membranes), the sodium chloride excreted is diminished to about $\frac{1}{100}$ of the ordinary amount. This is due, first to the restricted and almost saltless diet of the sick; 2nd, because in the serous exudations and watery stools much salt is withdrawn from the organism, and finally because of the diminished excretion of urine in all fevers. The only exception to these rules is intermittent fever, in the intermissions of which there is often good appetite, and an ordinary digestive power. If, in an acute disease, we find the sodium chloride excretion rising, it indicates a dimunition in the severity of the disease. In chronic diseases also, as a result of the diminished digestion of food, and the decreased tissue metamorphosis, the excretion of the sodium chloride is to a great extent diminished. In diabetes

insipidus, however, and during the absorption and cure of dropsies, the amount of sodium chloride present in the urine is increased to over 50 grms. per day (Vogel).

2. *Particular Facts.*—Under this head we shall consider the influence of medicinal and toxic doses of sodium chloride upon the individual organs and functions.

Skin.—It has been positively determined that no sodium chloride, as far as can appear in tests, is absorbed by the skin from baths, and that there is no increase of the sodium chloride in the urine from this cause. All the kitchen salt contained in the epidermis can, later on, be washed out again (Beneke, Valentine, Roehrig). But it was noticed that after the sodium chloride baths the amount of urea excreted was increased (Clemens, Beneke). Roehrig also found that after salt and sea baths the oxidation processes in the body were surprisingly increased. The last observer explains this fact in what is certainly a very hypothetical manner. He thinks that the salt which has made its way into the epidermis withdraws the water from the superficial layer of the skin, and as a consequence the sensible nerve ends experience a shrinkage, which acts as an irritant, and in a reflex manner, by irritation of the vaso-motor apparatus, causes a narrowing of the bloodvessels and an increase of the blood pressure; the result of this is the increase of the tissue metamorphosis, augmentation of the urea and carbonic acid excretion and a rise of temperature. The slightly irritant effect of salt baths is due to the extensive shedding of the epidermis which follows them, and the pustular inflammation of the skin thus produced; these pustules in former times were considered as "Badekrisen" (Bath crises).

Digestion and the Digestive Tract.—Sodium chloride has the typically salty taste, and produces upon the mucous membrane of the fauces a sensation known as "thirst." This sensation is probably only partly due to the fact that the sodium chloride (contained in the food and drink) in passing through the pharynx absorbs water from the mucous membrane, thus producing an irritation of the the sensitive nerves of the mouth and œsophagus. For, in the first place, the local action of the sodium chloride upon these nerves is of very slight duration. Secondly, if this were the sole cause of the "thirst" it should set in immediately, or at least sooner than it does, after the salt has been swallowed; finally the experimental fact that thirst follows the subcutaneous injection of salt is opposed to this theory. According to Heubel, the chief cause of the thirsty sensation following the taking of salt is that the sodium chloride

which is absorbed into the blood and remains there in simple solution, and not combined with any albuminoid body, withdraws water from the tissues of the body, especially from the mucous membranes of the digestive tract, and thus produces a dryness of these mucous membranes and the sensation of thirst. The water thus abstracted from the tissues is excreted with the sodium chloride by the kidneys. The water which is instinctively taken in consequence of the thirst leads to a dilution of the chyle and thus to its easier absorption, increasing the fluids carried to the organs, and thus leading to an increased tissue metamorphosis. A further consequence of the irritation of the nerves of the mucous membranes of the digestive tract (especially mouth and stomach),is the reflex increase in the secretion of saliva and gastric juice, and again as a result of this the more rapid digestion, both of the starchy materials of the food (rapid conversion into sugar by the saliva) and of the albuminoids (rapid peptonization.) According to Lehman, even in artificial gastric juice, (and thus without reckoning the increase in quantity), coagulated albumen and coagulated fibrine are more easily dissolved when 1.5 per cent. of kitchen salt has been added; a larger quantity, however, interferes with the peptonization. In the intestine the solution of the fibrin, by means of the pancreatine, is hastened by the addition of sodium chloride (Haidenhain). When albuminous solutions were injected into the large intestines they produced an increase in the secretion of urea only when sodium chloride was added to the injection (Voit, Bauer).

Large quantities produce a severe inflammation of the stomach and intestines,* with severe pains, vomiting and diarrhœa, sometimes followed by death (when 500–1,000 grms. are taken.)

Kidneys and Urinary Excretion.—According to Voit and Falck a considerable increase in the excretion of urine is produced in dogs after too great an absorption of sodium chloride and when the normal percentage of salt in the blood is passed.

Observations upon men contradict these results; only when much water is drunk with the salt is the urine increased; it is diminished, if the sodium chloride be taken without an increase in the amount of water absorbed (Falck, Klein, and Verson).

The observation of Wundt that when sodium chloride is withdrawn from the diet the appearance of albumen in the urine follows, has not yet been confirmed by any one and can therefore only be considered as an accidental compli-

*Compare statement page 28.

cation. The statement of Plouviez that albuminuria can be cured by sodium chloride also requires further evidence to obtain credence. The circulatory system, the respiration, the temperature, the nerves and muscles in men and animals are not visibly affected by the administration of medicinal doses. The administration of toxic doses, however, in a series of experiments upon animals has brought to light a number of noteworthy effects.

Poisonous Effects of the Sodium Chloride in Animals.—In the introduction to the alkalies and when the general sodium action was considered, we hinted at several of the effects of sodium chloride. These we shall here repeat with greater completeness, since there are some differences between sodium chloride and neutral sodium salts.

On Cold-Blooded Animals.—After the administration of large quantities of kitchen salt, according to Kunde, frogs fall into severe tetanoid convulsions; (when a nerve is placed in concentrated solutions of kitchen salt it throws its muscles into a tetanic convulsion.)

Then the animal excretes a quantity of fluid through the skin, a sort of perspiration, so that sometimes the water gathers in drops upon the skin. During this time the strength of the animal diminishes, sensibility and motility disappear, until finally the heart ceases to pulsate. The nerves and muscles have then lost their irritability. The decrease in weight caused by the loss of water is considerable.

If the salt be injected hypodermically we find no change in the intestinal canal; a large quantity of fluid, however, collects under the skin. Introduced into the stomach it produces considerable hyperæmia of the mucous membrane, appearances of a bloody mucus in the stomach and intestines, and vomiting. The animal soon stops breathing. Introduced into the rectum it causes an extensive transudation of water into the intestinal tract.

According to Falck-Hermanns dilute solutions of sodium chloride (½ %) increase the frequency of the action of the frog's heart which has been cut out of the body (if applied immediately after the heart has been cut out); but strong solutions cause a more rapid cessation of the heart's action, for they interrupt it immediately.

If a frog is kept in a concentrated solution of sodium chloride for any length of time, fibrillary muscular contraction takes place, but no general convulsions (Guttmann).

Stricker—Prussak have seen in frogs, after an injection of

sodium chloride, a migration of the red blood globules from the uninjured capillaries, which was often so strong that the whole skin appeared dotted red. Cohnheim has, on the other hand, observed that a similar emigration of blood globules takes place in all frogs at a certain period of the year. Kunde has observed that shortly after the introduction of from 0.2 to 0.4 grms. of sodium chloride under the skin or into the rectum of frogs, there appears a swelling of the cornea, an increase in the amount of the aqueous humor, and a cloudiness of the lens, which sometimes begins upon the anterior and sometimes upon the posterior wall. Finally the lens appears of a light ash color. All these phenomena disappear when the animal is placed in water.*

Most of these phenomena in the frog can be explained by a withdrawal of the normal amount of water.

Warm-blooded Animals.—Guttmann observed, after the injection of 5 grms. of sodium chloride in rabbits, clonic and tonic spasms, which did not occur, however, in animals who received water at the same time. Death occurred, however, in spite of the respiratory function and heart's action remaining intact. According to Falck, poisoning produced by the injection of sodium chloride into a vein causes particularly characteristic changes in the organs of respiration, a discharge from the mouth and nose and constant dyspnœa. Kunde also observed that sodium chloride produced in living cats a cloudiness of the lens (with the well known star-shaped figure upon the surface). Guttmann, on the other hand, denies that cataract can be produced by the administration of sodium chloride to warm-blooded animals. †

THERAPEUTIC APPLICATION.

That sodium chloride is one of the most important of the salts necessary to nutrition, and that its supply to the organism is indispensable is evident from a consideration of its physiological action. For this purpose, however, it is not introduced medicinally but rather in the food as a necessary addition.

Medicinally, however, sodium chloride is extensively used internally, both for various individual conditions, which we will soon mention, and for which generally one dose of the salt is sufficient, and principally as a "drink cure" in the form of

* Compare p. 20.

† Compare p. 20.

natural mineral waters containing sodium chloride, for chronic diseases.

Sodium chloride is administered under the following circumstances. In hæmoptysis as a hæmostatic; for this purpose the remedy is even used by the people, and, as experience teaches, one that is often successful. One to three teaspoonfuls of sodium chloride, taken dry or with a little water, will often stop even a somewhat profuse hæmoptysis, especially if the proper dietetic precautions are observed. Sometimes nausea is caused by it, in other cases none. The hæmostatic effect is dependent upon the fact that the salt produces a severe irritation of the sensitive nerves of the stomach, which causes a reflex contraction in distant arterial vessels, as, for instance, in those of the lungs. We have several times observed that in cases of epilepsy, where the attack is preceded by a so-called aura arising from the stomach, that is to say in the distribution of the vagus, and where the period between the aura and attack is long enough, the swallowing of one or several teaspoonfuls of salt will sometimes ward off an attack. Its utility in intermittent fever (Piorry and others) and cholera (internally or injected into the veins) has not been confirmed.

Sodium chloride is further utilized as an antidote to *argentic nitrate*, especially if a large quantity of this substance should get into the stomach, as happens accidentally when the *argentic nitrate* is used for affections of the throat. The resulting argentic chloride is not absolutely insoluble, but this antidote should always be tried because always at hand. When leeches are accidentally swallowed they can be killed by drinking solutions of salt. Sodium chloride is even yet often used as an *anthelmintic*. It is entirely uncertain that it is effective against the tape worm or thread worm. Experience, however, teaches that it is a good plan to administer sodium chloride (generally in the form of a salt herring) before the real anthelmintic, upon which we depend, is administered.

When sodium chloride is to be used continuously for a specific therapeutic purpose, we make use of the natural sodium chloride mineral waters. Sodium chloride is present as an ingredient in very many mineral waters; in some it forms the chief active component, in others its influence is secondary but appreciable, as in the alkalies, alkaline muriatic, in the Epsom and Glauber salt waters. As we would expect, the therapeutic indications for the use of natural springs in which the chief ingredient is sodium chloride, are the same as those already recounted as indicating the use of the other springs. These are:

Chronic Dyspepsia and Chronic Gastric Catarrh.—As to particulars, we have already mentioned them in speaking of the alkaline carbonates; we do not know of any additional facts which should be mentioned here. Perhaps experience is in favor of the use of waters containing sodium chloride and Glauber's salts in cases of which constipation is a prominent symptom. The springs most used are Kissingen, Homberg, Soden, Cronthal and Canstatt. In chronic intestinal catarrh the springs containing only or principally sodium chloride are not very much used. When carefully selected these waters might be used, but we should prefer Karlsbad, Tarasp, etc.

Certain kinds of Corpulence and so-called Plethora Abdominalis.—Experience has taught us that in people with a fat abdomen, relaxed muscles and pale skin, the sodium chloride waters, such as Kissingen and Homburg, should be preferred to the Glauber salt waters.

Chronic Bronchial Catarrh and Incipient Phthisis are often treated with a good result by the sodium chloride waters. That these do not possess the least specific influence over the phthisical process need not be stated; their action depends upon the climatic change which drinking these waters necessitates, and also upon the improvement of any bronchial catarrh or dyspeptic condition that may be present. We must be careful not to overestimate the value of these waters in phthisis; we do not conceal our opinion that its effect is due principally to the change of air and hygienic conditions. Of the many springs Soden in Taunus is most used for consumptives.

Whether in chronic enlargement of the spleen and liver, which are the result of malarial infection, the sodium chloride waters (Kissingen, Homburg) should be preferred to Karlsbad, is difficult to decide.

Even in *Gout* the sodium chloride waters are used, but for most cases Karlsbad and Vichy should be preferred. Garrod makes this distinction, that he considers the waters of Wiesbaden better fitted for the treatment of chronic forms of rheumatism than for true gout.

In scrofulous affections of different kinds, we use in addition to brine baths, which are here certainly of much utility, the sodium chloride "drink cure." Whether the latter are of any utility does not appear beyond doubt; besides that, their use is limited, because the treatment can not be carried out in children, in whom most of these cases occur; if used at all we must employ the weaker waters and those containing at the same time carbonic acid (Homburg, Kissingen, Canstatt).

The utility of sodium chloride waters for the reabsorption of pleuritic and other exudations, which are the result of chronic inflammatory processes, is exceedingly doubtful. Here again, the altered hygienic conditions probably play a chief part in the good effect.

We now turn to the external application of sodium chloride. In this connection we may mention that it is used as an addition to clysters. Salt clysters are those most frequently prescribed as a cathartic. The method of its action is evidently by the production of peristalsis through irritation of the nerves of the mucous membrane of the rectum. According to some it is good practice as a secondary precaution, when no other agent is at hand, to wash poisoned wounds with solutions of salt; primary means being acetic acid in light cases and energetic caustics in serious wounds. Weak solutions of salt are further used to neutralize the superfluous argentic nitrate, when this caustic is applied locally to the conjunctiva.

To produce a slight irritation of the skin salt-water is one of the most useful means; it is therefore added to foot baths, to vaginal injections, and applied, dissolved in alcohol, to parts affected by muscular rheumatism. Most of all, however, salt baths are used locally as methodical bath cures in the form of "brine baths."

The indications for the use of brine baths were formerly very numerous. Experience has however reduced these, so that any real utility is only expected in the following cases.

In *chronic rheumatism* of the muscles as well as of the joints, these are useful; but in arthritis deformans we have never seen any benefit follow from the use of this salt. From what we have said, however, we would not have it understood that sodium chloride baths are of more service in an ordinary case of rheumatism than thermal or steam baths and others, but simply that they are of utility in these affections.

In abnormal sensitiveness of the skin to the influence of the weather and the extremes of temperature, we sometimes use salt baths, and in these cases the hot salt baths, rich in gases, as those of Nauheim and Rehme.

The employment of salt baths in scrofulous affections of all kinds is very general; and really good results follow, but we must not forget that in addition to the cooking salt, there are many other important factors which help to produce the good effects. The model of natural salt baths for these affections is Kreuznach. According to more exact observations the iodine and bromine take little share in the effect of salt baths. Several

[illegible]

[illegible] chloride is found in many natural [illegible] substances, upon which [illegible] depends [illegible] is principal [illegible] spoken of under the name of sodium [illegible] waters.

[illegible] sodium chloride springs used for drink[illegible]. It is evident that both varieties may [illegible]. Experience has taught us to use those [illegible] contain in addition to the sodium chlor[illegible] carbonic acid.

[illegible] chloride drinking waters are 1. Kis[illegible] carbonic acid cold drinking waters are [illegible] (about the same proportion). Max [illegible] are not worthy of consideration. 2. [illegible] springs, with a temperature between 15–25° [illegible] from 0.2–1.3%; a somewhat large

proportion of carbonic acid. A slight percentage of iron is not taken into consideration. 3. Homburg on the Taunus, cold, quite rich in CO_2—slight proportion of Fe., the springs are Elizabeth springs (about 0.9% of Nacl and Kaiserbrunnen about 1.4%). 4. Nauheim on the Taunus, principally used as a bath; for drinking purposes the cooler springs, and those containing a medium quantity of CO_2 are used. Very rich in sodium chloride. 5. Cronthal on the Taunus—about 0.3% of sodium chloride and a similar percentage of CO_2. 6. Neuhaus in Franken—cold—equal amounts of CO_2 and NaCl., about 0.6–0.7%. Mergentheim in Würtemberg—cold—little CO_2, about 0.6–0.7% of sodium chloride, and 0.2–0.25% of magnesium and sodium sulphate. 8. Canstatt near Stuttgart; a slight proportion of CO_2—little sodium chloride, about 0.2%. 9. Adelaide Spring in Heilbrunn, in Bavaria—0.4% of sodium chloride, a small amount of carbonic acid and sodium bicarb. 10. Wiesbaden—province of Hessel-Nassau—is also used for bathing purposes: the drinking spring hot (69° C.), contains little carbonic acid and about 0.6% of sodium chloride. All other springs of Wiesbaden are of a high temperature.

Various springs are used for drinking purposes and generally in most salt baths, a water fit to drink is manufactured by the addition of carbonic acid and a proper dilution with water. Those most mentioned are the natural sodium chloride drinking springs most used in Germany.

Sodium chloride bathing springs—brine baths. The waters just mentioned are often used as baths, but they are only fitted for this purpose when mixed with a sufficient quantity of salt, because they contain so little salt originally. The same is true of some of the waters used for baths.

We can not here enter upon a detailed discussion of each individual German bath; but again must limit ourselves to merely mentioning these, with brief notices appended. In addition to those already mentioned we have 11. Baden-Baden—in Baden—46–68° C. 12. Soden near Aschaffenburg. 13. Schmalkalden in Thuringian Forest. 14. Sulzbrunn in Bavaria. All of these baths contain little sodium chloride.

The strong brine baths are 15. Kreuznach in Nahethal. 16. Arnstadt in Thuringia. 17. Salzungen in Meiningen. 18. Frankenhausen in the golden meadow. 19. Sulza in Weimar. 20. Kosen in Naumburg. 21. Koestritz in Raus. 22. Wittekind, near Halle. 23. Colberg in Pomerania. 24 Pyrmont in Waldeck (ferric waters compare.) 25 and 26. Harzburg and Suderode on the Harz. 27 and 28. Jaxtfeld and Rothweil on the Neckar. 29. Hall, in Wurtemburg. 30 and 31. Goczalkowitz and Königsdorf—Jasrtzemb in Silesia. 32. Hall near Linzin, Austria. 33. Aussee in Steiermark; 34. Hall, near Innsbruck, in Tyrol; 35. Ischl, in Salzkammergut; 36. Reichenhall, in Bavaria. In addition there are various smaller brine baths, and in some places where the spring waters may be used in some other way, the sodium chloride is used as an accessory. As to other details we must refer to special works on Balneotherapy.

Rehme (Oeynhausen), in Westphalia, and Nauheim take peculiarly prominent places among the brine baths, they being considered thermal brine baths rich in carbonic acid. Soden is the nearest approach to them.

Concerning the proportion of Iodine contained in these springs, compare with what is said under Iodine.

Sea baths must also be mentioned here, because of the amount of sodium chloride contained in them. In these, however, we must consider other factors in estimating their curative value, such as the sea air, the low *temperature of the bath*, besides the physical influence of the force of the *breakers*.

As a principal indication for the use of sea baths we have the following negative circumstance, that only such individuals should make use of them as are suffering from no decided organic disease. The pathological conditions for which sea baths are indicated are as follows :

All of the physiologically ill-defined conditions of general weakness, in which no decided organic trouble is present, and which are rather due to neurasthenia resulting from mental overwork, or are the sequelæ of acute or chronic maladies, or which appear as a symptom of inefficient assimilative functions.

Furthermore many persons suffering from what is generally known as nervous debility, of which we cannot here give an accurate clinical picture, find the sea-baths of great utility.

These baths are also excellent in the so-called "cutaneous sensitiveness" with a tendency to take cold readily, and abnormal sensitiveness of the skin. They are also followed by good results when used in chronic muscular rheumatism and even in rheumatic joints after all other therapeutic means, such as other baths, have been used.

Finally they are indicated in some forms of scrofula, especially when no severe localized lesion, such as enlargement of the lymphatics are present.

Further it is necessary to remark that as a general rule very pale, anæmic and ill-nourished individuals, with poor assimilative power, bear salt baths very badly and in these they must be used with great precautions.

The relative proportion of sod. chloride present in the Atlantic Ocean, North Sea and Mediterranean is about the same (about 2–3 %). Much smaller in the Caspian Sea (about 1 %). The sea waters of the south, which are of interest to us, are in general 5° C. warmer than those of the north. The force of the waves is also of great importance. This varies with the situation of the beach and the direction of the wind during the bathing months. Finally it is of some moment whether the beach be situated upon an island or not. Those upon an island generally combine most of the good qualities of sea water bathing.

The most commonly used sea-baths are :

Baltic Sea—Cranz, Kuren, Zoppot, Ruegenwald, Colberg, Dievenow, Misdroy, Swinemuende, Heringsdorf, Puttbus and Sassnitz on Ruegen. Warnemuende, Travemunde, Doberan, Duesternbroek, Marienlyst.

North Sea—Ostende, Blankenberghe, Scheveningen, Heligoland, Cuxhaven, Westerland upon Sylt, Wyk upon Foehr, Borkum and Norderney.

Atlantic Ocean—Duenkirchen, Dieppe, Boulogne, Havre, Trouville, Biarritz in France ; Dover, Wight, Brighton, etc., in England.

Mediterranean Sea—Marseilles, Nizza, etc., in France ; Spezzia, Livorno, Naples, Venice, etc., in Italy.

POTASSIUM CHLORIDE—POTASSIUM CHLORATUM.—CHLORINATED POTASH.

Concerning the importance and physiological action of potassium chloride or chloride of potash, KCl, we were compelled to say so much in considering the action of potassium as well as of sodium chloride,* that we would only refer to what was said above, again calling attention to the fact however that the action of potassium chloride is principally one of potassium. A favorable effect upon epilepsy, similar to that following the use of potassium bromide has been noticed by only one observer (Sander), while others have denied it.

Therapeutically it is not used.

* See pages 15, 16 & 18.

POTASSIUM CHLORATE—POTASSIUM CHLORICUM.

The potassium chlorate $KClO_3$ still bears the antiquated name of chlorate of potash and potassium chloricum in the pharmacopœia. It should not be confounded with potassium chloride, KCl, the old name for which, chloride of potash, potassium chloratum, might easily lead to this.

The potassium chlorate forms white, shining, scaly crystals, which dissolve in 16 parts of cold and three parts of boiling water and have a cool saltpeter-like taste. With most oxidizable substances (such as sulphur, carbon, etc.,) it forms solutions which under concussion will explode.

PHYSIOLOGICAL ACTION.

In medicinal doses (5.0 grms. daily) it is rapidly absorbed, passes into the circulation without change and soon appears in all of the secretions (urine, saliva, tears, milk, sweat and bile). Within 36 hours all of the salt that has been administered is thus excreted from the body. (Isambert and Hirne found 95–99 % returned by the excretions.)

When administered for any length of time in medicinal doses (10.0 grms.) we observe an increased production of saliva, the cause of which is doubtful ;—it is uncertain whether it is due to a direct action of the salt upon the salivary glands or as a reflex result of the irritation of the nerves of taste ;—we have also a feeling of hunger produced, increased excretion of a strongly acid urine with pain over the kidneys ; the stools are green in color. Diarrhœa is not produced even by large doses.

Very large doses have been considered fatal, in that they are liable to produce death by paralysis of the heart just as other potassium salts. But it has been said that adults have received 30.0 grms. without any harm resulting therefrom.

Lately, however, Marchand, in Halle and Jacobi, of New York, report fatal poisoning of children caused by this popular remedy. Death set in either suddenly with a sepia-brown color to the blood, and without any evident organic lesion, or after several days, with symptoms of kidney disease, which were evident during life, excretion of a dark brown urine, containing many disintegrated blood corpuscles. The pathology of this disease is not an inflammation of the kidneys, but an obstruction of the uriniferous tubules by the blood corpuscles.

Even in experiments on dogs, which were killed by a 10.0 grm. dose, Marchand found similar alterations in the blood ; (the blood, as the poisonous operation advanced became dark, and lost its *capability* of reddening when shaken with air ; *at this stage death* set in without any other alterations ;) he

also found a similar obstruction in the tubules of the kidneys. The cause of this brown color of the blood seemed to be the formation of methæmaglobin, into which, as is well known, oxihæmaglobin is changed by all oxidizable substances.

Marchand therefore warns us against the use of potassium chlorate in very weak children. Sodium chlorate has a similarly bad effect and should also not be administered.

Pus, yeast and fibrin deprive potassium chlorate which has been dissolved in water of its acid, and reduce this particularly rapidly when applied in a putrefying condition.

THERAPEUTIC APPLICATION.

Potassium chlorate is chiefly used in some of the affections of the mouth. *Stomatitis Mercurealis*, with or without ulceration, is the affection in which this salt is the most useful and best remedy that we possess. The symptoms of gingivitis disappear and the ulcerations heal more rapidly, but the mercurial salivation is not influenced by this remedy. Potassium chlorate is an excellent prophylactic against the appearance of mercurial sore mouth during a course of inunction, etc. For this purpose the salt should be taken internally and locally as a mouth wash, beginning at the same time with the inunction. We are more doubtful of the effect of potassium chlorate in aphthæ (stomatitis aphthosa), it may, however, be tried if too great pain is not caused by its application. It is entirely useless, however, in thrush although many physicians use it for this purpose.

That the remedy is entirely useless in diphtheria when given in the ordinary doses hardly admits of any doubt. Some physicians (Seeligmueller and Sachse), however, prescribe and recommend as very useful a saturated solution (5 per cent.); it is to be given at first every hour, then every 2 or 3 hours ; at first without any intermission day and night. No corrective should be added to the watery solution. Children over 3 years should receive tablespoonful doses, with now and then only an ordinary teaspoonful dose. Jacobi and Marchand, on the contrary, advise strongly against such large doses, which they consider dangerous (compare with physiological portion).

The abuse of potassium chlorate in affections of the mouth, is carried so far that it is often used in catarrhal angina ; its utility in these cases is entirely illusionary.

This remedy has also lately been used as an antiodontalgicum *(E. Neumann.)* It is entirely without effect in toothache, due

to periostitis of the root and alveoli ; but good in inflammation of the pulp when the latter is exposed through caries of the teeth ; less effective when the carious opening by which the exposed pulp communicates with the outer air is small. How to explain the favorable action of potassium chlorate in this connection is difficult to say—perhaps it is the simple nerve effect of potassium. Edlefsen has lately reported excellent results from the use of potassium chlorate in catarrh of the bladder, whether acute or chronic. We have not yet been able to confirm these observations by our own experience. Of the many other recommendations for the use of this salt, most of which are unreliable, we shall only select two. Older physicians assure us that the remedy can often be used with good effect, after every thing else has failed, in neuralgia of the fifth. We are not able, as we have just hinted, to particularize any cases. Were not these neuralgias due to a carious process of the teeth? Burrow recommended the daily powdering of open cancerous sores with potassium chlorate in powder or crystals. It is said the growth shrinks and diminishes, and that neighboring infiltrations are absorbed, the secretions (of the sore) and sensitiveness being diminished. The scarcity of reports concerning this use of the salt, does not permit of any conclusion. (Vidal uses in addition the long continued internal administration of this remedy.)

Dosage, Potassium Chloricum.—Internally from 0.1–0.5 per dose (5.0 per day) only in solution. On account of its explosiveness not in pills or powders. Externally as mouth wash (5.0–10.0: 150–200.0) or throat application (5.0 to 30.0 honey and 30.0 water.)

7.—THE ALKALINE NITRATES.

SODIUM NITRATE—CHILI SALTPETER.

The nitrate of sodium—sodium nitrate ($NaNO_3$) which is found in large quantities in Peru, presents in a purified state, colorless transparent rhombic crystals, has a saline, cool taste, and is soluble in 2 parts of cold and 1 part of hot water.

Physiological Action.—Death occurring in many cases of oxen, horses, sheep and swine, that had accidentally drunk water containing chili saltpeter, induced Barth to undertake a new series of experiments upon animals.

He considered, partly from the results of Gscheidlen's and Schonbein's experiments, that sodium nitrate ($NaNO_3$) was partly reduced in the intestinal canal and (from *his own* experiments) partly in the tissues by means of *muscular action, to sodium* nitrite (Na_2NO).

Pancreatic juice seemed to facilitate the reduction—and the bile to hinder

it. In the urine the nitrite is often but not always present. The nitrite is, however, much more poisonous than the nitrate, and produces, even in relatively smaller doses (0.1 in rabbits of 500 grms., 0.5 in dogs of 3,000 grms. weight), vomiting, general depression, muscular twitchings, salivation, increased urinary excretion, thin fæcal movements, alteration in the color of blood, and death. The action of the nitrates is, therefore, dependent partly upon the nitric acid which is liberated in the tissues, and, therefore, the physiological action of the sodium nitrate is in no way a pure sodium action.

Even if we were to acknowledge that the nitrate is really converted into the nitrite, it would, according to our opinions, be of little consequence, for Barth, in contradiction to his own theories, proves that sodium nitrite is much more poisonous than the nitrate.

Otherwise his statements concerning the general effect agree almost entirely with those of Guttmann, that smaller doses have no particular effect, while large doses produce death with symptoms of simple asthenia, no evident symptoms of a disturbance in respiration, circulation or bodily temperature, being present; the heart ceases to beat some minutes after respiration has ceased.

The narcotic effect upon the central nervous system which he, on the other hand, lays great stress upon, and which he says is shown by stupor, diminution of reflex action, etc., has not been seen by other observers; Guttmann, indeed, plainly denies that any such action can take place. [Compare page 9.]

Loeffler gave healthy 20 year old men 90–150 grms. of Chili saltpeter in 8–14 days (3–15 grms. daily), and found, after the administration of 90 grms. in 8 days, scarcely any abnormal symptoms, but found, after continued administration beyond this time, that a *feeling* of *general weariness* set in, which was increased upon motion, and which continued for several days after the giving of the salt had been suspended. There was a lack of bodily and mental energy, depression of spirits, weariness upon the slightest exertion, with a feeling of soreness in the muscles and joints, sleepiness, and yet they gained no strength or refreshment from sleep.

In addition, the *pulse became weaker*, *softer* and *slower*. Toward the end of the experiment the face became paler and thinner—wounds healing more slowly. Digestion was, however, very slightly disturbed, and the appetite remained equally good. Only twice after long continued use was there intestinal pain and rumbling in the intestines. *Bowels* were *normal*, perhaps *slightly constipated.*

The excretion of urine, reported by Lœffler as not without doubt increased, was found by Schirks increased in the beginning, after a few days of normal quantity and sometimes falling below the normal.

The blood, which Loeffler withdrew from the veins of the poisoned individuals, upon whom he experimented, showed a cherry juice color, increase and enlargement of the colorless blood corpuscles, a deeper color of the red blood globules. More rapid coagulating power, increase in the proportion of water and salt, diminution of the solid constituents and fats.

Older and more recent observations (on men and animals), thus agree in the conclusion that even proportionately large doses (in men up to 10 grms.) produce no particularly abnormal symptoms when given for 8 days, but later and in larger doses produce poisonous effects which have the character of those produced by sodium, which we recounted in the introduction. Even the latest contribution of Barth, although written from an opposite standpoint, does not prove any sensible difference.

Therapeutic application.—We consider sod. nitrat. as an entirely un-

necessary drug clinically. The salt was administered for many years to serve the same indications as the corresponding potassium salt. If the latter is entirely untrustworthy, the sodium salt is certainly so; and this is becoming more and more the general professional opinion.

Formerly, we ourselves administered the remedy in many cases without any noteworthy effect.

Dosage.—Sodium nitricum, 0.5–2.0 per dose (15.0 per day) in solution.

POTASSIUM NITRATE, POTASSIUM SALTPETER.

The purified potassium nitrate (KNO_3) forms large rhombic crystals of a cool, salty taste, and great solubility (in 4 parts of cold and 1 part of hot water.)

Physiological Action.—Inasmuch as the action of large toxic doses, which have been rapidly introduced into the circulation, is very similar to that of potassium, which was treated of in the introduction*), we shall here speak only of the effects of internal medicinal doses in man.

Small quantities (about 0.5 grms.) when given once produce, apart from the cooling taste, no noteworthy effect. When long continued the appetite is lessened, bowels constipated, and urine increased. Some describe a kind of scorbutic condition as a result of the long continued use of this salt. Saltpeter that has been entirely absorbed is rapidly excreted by the urine.

Larger quantities (up to 5.0 grms.) taken in substance or in very concentrated solution, cause a dryness of the mucous membrane of the mouth and pharynx together with excessive thirst, burning in the epigastrium and eructations; in dilute solution, however, no local symptoms are observed, but we have an increase in the amount of urine, with a higher specific gravity; in some diarrhœa occurs, in others constipation.

Pulse and temperature are not influenced by such doses as these, but are lowered by large toxic doses, which cannot be administered to men, because they cause a *toxic gastritis* in consequence of the intense diffusion current which takes place (see page 18), accompanied by severe pain, vomiting and purging. All of these symptoms, such as great weakness, fainting, uncommonly weak circulation, and death, have, for a time, been ascribed to the specific action of the potassium, because this is one of the most readily diffusible of the potassium salts, but, as we have already shown, the gastritis is probably as active in the production of these symptoms as the potassium which is absorbed.

Hence the impossibility of using saltpeter as an antipyretic. Although very recently the use of potassium nitricum is very much recommended in articular rheumatism (Leube Gerhardt.) Large daily doses (50 grms.) would be pretty well borne, if they are well diluted, seldom only vomiting sets in. Yet, if the cases observed in Gerhardt's clinic be studied, we shall find that the reduction in temperature did not take place until the salt had been used for several days (in 3 cases 3 days; in 4, 6–9 days; in 1, 11 days; in 1,17 days; in 1,18 days; in 1, 22 days and in 1, 30 days,) so that it is pretty difficult to be convinced from these observations that the nitre was the cause of the reduction of temperature. Even the observation that the fibrin of the blood is dissolved in 10 per cent. saltpeter solutions, and that in cases of poisoning by the salt the blood is with greater difficulty coagulated, cannot alter our opinion, for many other salts of potassium and sodium have a similar effect, and we *do not know that* the formation of fibrinogenous materials in the

* See page 21 and following.

living circulating blood is prevented by the administration of saltpeter; in addition to this we would say that the old theory of Swieten, that death from high bodily temperature is caused by a coagulation of the fibrin of the blood, upon which the theory of the antipyretic action of saltpeter is founded, is no longer tenable. For most of the cases of death from elevated temperature show only a small percentage of fibrin in the blood and produce a soft coagulum.

Samuel's experiments, in which he believes to have shown that the inflammatory symptoms produced by croton oil upon the ear of a rabbit, are best prevented by saltpeter, need further confirmation.

The experimental researches, to explain the diuretic action of saltpeter have not yet led to any thing further than that it renders membranes more permeable to water, and that the saltpeter in passing through the kidneys, draws a quantity of water with it. Concerning the absorption of this salt with and excretion from the blood, Hermann Forel has shown upon rabbits, that the whole quantity introduced into the stomach is absorbed, but not so rapidly as was supposed; that no trace of it is found in the intestinal contents, or in the fæces, and that the dose absorbed into the body does not leave with the urine until two days have passed.

Therapeutic application.—Potassium nitrate was formerly very much given in acute inflammatory febrile affections. Later on it was replaced, through Rademacher, by sodium nitricum, and lately physiological investigations have again led to its use in these diseases.

We must premise that according to our experience, which is in accordance with that of many observers, potassium nitrate is, for this purpose, an entirely superfluous drug. Given in the ordinary small or medium doses by the mouth, it acts neither as an antipyretic nor antiphlogistic; in very large, active doses it produces additional disagreeable gastric symptoms, and is certainly better replaced by quinine, sodium, salicylate, etc.

The theoretical points upon which the antiphlogistic and antipyretic application of saltpeter is based, have been discussed under the head of physiological action, and have been proved untenable or unsatisfactory. The remedy is generally used in pneumonia, pleurisy, endocarditis and pericarditis; also in acute articular rheumatism with especial favor; and finally in the acute febrile exanthemata, etc. As to the real benefit of the remedy in these affections, we are taught by an impartial criticism of the already detailed experiments (which alone is of value in such a study), and by our own extensive experience, the following facts. That saltpeter does not influence the course of the disease, nor does it in any way limit the spreading of the affection or to any degree affect the local process.

The chief symptoms of fever, the elevated temperature and frequent pulse are in no way affected by ordinary doses (0.5–1.0.) The uselessness of these doses, which when injected into the veins are fatal to dogs, is seen when they are given by the stomach. Small doses then are entirely without effect. Large ones, however, can reduce the temperature and pulse. These were most given in acute articular rheumatism, by some observers even up to 50 or 60 grms. per day. But even in these doses we do not, even in the majority of cases, find a real shortening of the duration of the disease, or an appreciably more rapid recovery from the local symptoms (compare page 66), and furthermore it has appeared that such large quantities sometimes cause toxic symptoms. Under any circumstances we have to-day a better remedy *for acute rheumatism* in salicylic acid. If large doses are administered then *it must be in a large* quantity of water, not in substance or concentrated solution.

Potassium nitrate is decidedly contra-indicated in acute inflammatory affections of the stomach and intestinal canal and the urinary organs, (Nephritis, Cystitis.) In the inflammatory affections mentioned above it should not be administered when any serious gastric affection is present, or where there is great prostration. It was for the latter reason that Tissot, Stael and others advised that this salt should not be given in putrid or bilious fever. A further application of potassium nitricum is as a *diuretic*. Its use presupposes that no inflammatory condition of the kidneys exists, and it should, therefore, be avoided in acute nephritis. In chronic nephritis we have not seen any disadvantage follow its use, but on the other hand never an evident and incontrovertible increase in diuresis. Immermann certainly believes that this does follow the use of potassium acetate. Saltpeter is furthermore of secondary value in the form of dropsy which occurs during the stage of compensation for valvular diseases of the heart, or in old chronic catarrh of the lungs with emphysema; cases in which it is chiefly important to increase diuresis by a rise in the arterial pressure. Here this salt may be added to prescriptions for other remedies, especially digitalis. Saltpeter is useful, however, (in addition to other treatment directed against the cause of the disease) in dropsy which is the result of a hydræmic condition. The salt is also much used when we wish to absorb inflammatory exudations as of pleurisy or pericarditis by an increased diuresis. We do indeed see the amount of urine increased under its use, after the febrile movement has disappeared, although we can not positively answer the question whether this is *propter hoc* or merely a coincident increase in the urine. When we observe that at this stage pleuritic exudations are diminished while a copious excretion of urine takes place, without any medication, we learn to doubt the utility of potassium nitrate. In hæmoptysis its utility is entirely illusionary.

Externally: Formerly saltpeter was often prescribed in cooling lotions—but now it need scarcely be used, for should we desire a lower temperature than we can obtain from ice we can accomplish it by the ether spray with better effect.

Dosage and preparations—1. Potassium nitricum—internally 0.3–1.0 per dose in solution or powder—but much larger doses have been given—up to 50.0 per day in large quantities of water. For cold lotion 15.0–30.0 to 500.00. The Schmucker fomentations formerly very much used were composed of 3 parts of saltpeter, 1 part of sal ammoniæ or cooking salt, 6 of vinegar, 12–24 of water. The salts were first mixed together, placed between cloths, adjusted over the proper place, and the fluid mixture poured upon it.

2. Pulvis Temperans seu Refrigerans—1 part of potassium nitricum, 3 parts of tartarus depuratus, 6 parts of sugar—0.6–1.0 per dose—formerly given to allay nervous excitement. This is only illusionary.

3. Charta Nitrata—Paper impregnated with saltpeter—strips of this are burned and the vapor inhaled. Recommended for attacks of asthma and for the prevention of these attacks.

8. THE COMBINATION OF THE ALKALIES WITH THE FATTY ACIDS.

SOAPS—SAPONES.

When fats are boiled with potassium or sodium solutions we have formed glycerine while the fatty acid combines with the alkali and forms a salt.

Action—On the Skin—When mixed with much water the soaps are decom-

posed into insoluble acid and soluble basic salts. The superfluous alkali of the latter is capable of forming new soaps with new quantities of fat. The fats of the skin are thus saponified and together with the dirt which adheres, separated from the skin. The alkali thus liberated may, as we stated when considering caustic potash, soften the epidermis and produce an inflammation of the skin. The potash soaps exert a more intense action in this respect than do the soda soaps.

Internally administered two things may happen. Either they are decomposed, as the alkaline carbonates are, the base forming a salt with the acids of the stomach, while the fatty acid is liberated ; or a portion is absorbed unchanged into the circulation and there burned to an alkaline carbonate. The older assertions that the blood contains soaps must be a mistake, when we consider the proportion of potash salts which it contains. Blood serum produces a precipitate of potash soap, with a soap solution ; this precipitate soon crystallizes ; blood serum can therefore contain no soap. The direct examition gives only negative results (Rohrig). However this may be the action of soaps internally administered is partly that of the alkalies, which we discussed under alkaline carbonate, and partly that of the fatty acids, which are oxidized in the organism or changed into a glyceride, and deposited as fat.

The symptoms following the internal administration of larger doses are: Disageeeable alkaline taste, nausea, vomiting, diarrhœa, and diminution in the nutrition of the body.

Application.—The internal application of soap is entirely obsolete ; for one purpose it is still used, namely, to neutralize the poisonous effects of acids that have been swallowed ; here it is useful because at all times present as soap water. Soda soap is also used in the preparing of pill masses, to which they are added by the aid of a little alcohol. Externally, soaps are commonly used, as is well known, as the chief means of purification. Therapeutically they are used to effect a mild irritation of the skin in some chronic skin diseases, as for instance chloasma and chronic eczema. When used alone, however, they rarely produce a curative effect. However, the soaps are very well fitted to bring organic matters as iodine, glycerine, etc., in a practicable form in contact with the skin, as sodo-glycerine soaps. According to recent reports (Kappesser and al.) friction with green soap is said to have a surprising effect upon scrofulous enlargement of the glands. Mesenteric and cervical glandular tumors are said to become smaller and disappear after many other remedies have been tried without any result ; other scrofulous symptoms are also said to be favorably affected by it. As a remedy for scabies the potash soap is still in use. It certainly does not destroy the parasite as was formerly supposed, but is a very good accessory to the very best treatment which is now adopted (use of balsams), as well as to the older English and other methods of curing the itch.

By the rubbing in of green soap and bathing, the epidermis is loosened, the burrows are more easily opened, the access of the balsam to the burrows and parasite is easier. A bath should therefore first be ordered, during which the surface is thoroughly rubbed with green soap and the balsam afterwards rubbed in. As a wash to withdraw infectious matters from the skin or wounds soap is insufficient. The method which was lately recommended, that soap, acting as a vehicle for permanganate of potash, should be used in washing for purposes of disinfection is insufficient, because of the too rapid decomposition of the permanganate, and has therefore been abandoned. Soap, finally, is much used as a laxative, either in the shape of clysma (soap water) or, in children, as a soap suppository. Its action is most probably based upon a reflex excitement of peristalsis.

Preparations.—1. Sapo medicatus, medicinal soap; dry pulverizable sodium soap, white and having no rancid odor. For pill masses 0.3–1.0 as a dose for medicinal purposes.

2. Sapo oleaceus s. Hispanicus, s. Venetus, Spanish or Venetian soap; sodium soap containing some potassium.

3. Sapo domesticus—talc soap—white sodium soap which is rendered more slippery by a small percentage of potash.

4. Sapo viridis s. kalinus niger—black, green or semi-fluid soap—potash soap prepared with the merest kind of fat, and of a smeary consistency. Produces a stronger irritation of the skin than any other of the soaps.

* 5. Sapo-dentifricius—tooth soap, odontine—medicinal soap, with magnesia carbonica, talcum preparatum. Iris florentina and oleum menthæ piperitæ. A very useful agent for cleaning the teeth.

6. Spiritus saponatus—tincture of soap. A solution of sapo Hispanicus in alcohol and aquæ rosarum. Has a slightly irritant effect upon the skin, used in frost bites, rheumatic pains, etc.—only externally.

APPENDIX TO THE ALKALIES.

The following preparations are either replaced by those already mentioned, or superfluous, or their effect is too little known or their therapeutic action is misunderstood. They are: Sodium biboricum, borax, (formerly recommended as an emenagogue, and inciter of pains during labor, and still used for aphthæ and thrush of the buccal cavity.) It has lately been highly recommended for the latter affection by Edlefson-Kosegarten in pulverized form or in concentrated solution, because it stops the development of bacteria and the yeast cells.) *Sodium ethylo-sulphuricum (a cathartic similar to the cathartic salts.) Sodium chloricum (similar to the potassium chloricum); furthermore—*Potassium tartaricum boraxatum; the potassium sulphuricum sal polychrestum glaseri (carthartic like the corresponding sodium salt.)

Later, sodium lactate (in doses of about 15.0) has been recommended by Preyer as a hypnotic; its effects are pretty sure to follow after its subcutaneous injection or when administered by the stomach, provided that the mind is not disturbed by distracting thoughts. Theoretically even, statements such as these would lead us to doubt its usefulness. After having been tested in the most varied manner by v. Boettcher, in our clinic (Nothnagel) this salt has proved itself a very weak and exceedingly unreliable hypnotic, which can never for this purpose begin to replace either morphia or chloral.

The combination of the alkalies with chlorine, sodium, bromine, arsenic, antimony, ferro-cyanic acid, benzoic and salicylic acids, will be considered under these respective headings.

II. THE ALKALINE EARTHS.

The alkaline earths are weaker bases and caustics than the alkalies. In addition they are distinguished from the latter by the difficult or entire insolubility of a portion of their salts. The carbonates, phosphates, and with the exception of the magnesium sulphate, the sulphates of the alkaline earths are *scarcely or not at all* soluble, while the corresponding alkaline *salts are readily* soluble in water.

Of the four metals of the alkaline earths, that is calcium, magnesium, strontium and barium, only the two former give us therapeutically applicable preparations.

The carbonate and phosphate of calcium and magnesium are normal components of the animal body, and though found dissolved in the fluids of the same, have a more important function in the formation of the firmer tissue as the bones and teeth.

Internally administered the magnesium salts have a similar action to those of the alkalies. The calcium salts, however, reveal greater points of difference.

The injection of these salts directly into the blood produces a variable poisonous effect in cold and warm-blooded animals. The most poisonous are the barium salts, then come in a decreasing series the salts of magnesium, calcium and strontium.

The following are according to Mickwitz the chief toxic effects of the direct injection of the chlorides of these salts into the blood of cats and frogs:

Barium chloride produces 1.—a great increase in arterial pressure which is independent of any irritation of the vasomotor center in the medulla. Shortly before the death of the animal the blood pressure sinks to the zero point, while the pulse is quickened. 2.—It has an irritating effect upon the smooth muscular fibers of the intestinal and bladder walls, as well as those of the bloodvessels. 3.—It alters the functions of the nervous centers and produces in cold-blooded animals paralysis of sensation and motion, and in mammalians convulsions.

The peripheral nerves are altered after long continued action of the poison.

Calcium chloride increases the energy of the heart and quickens the frequency of the pulse in mammalians. Large doses have a paralyzing effect upon the heart. The functions of the nervous centers are weakened or entirely abrogated. Cats are thrown into a narcotized state (sleep), during which consciousness is entirely abolished, and even the most painful sensations call forth no reflex movement.

Strontium produces no particularly poisonous effect.

More complete experiments, which include the study of more combinations, must be made. As was the case with potassium, so here also we must especially call attention to the fact, that, although all of these effects produced by the direct injection of the salts into the blood are of the greatest theoretical interest, yet they must not necessarily be considered as the result also

of the internal administration of the drug. For these very experiments, as far as the most of the calcium and magnesium salts are concerned, are opposed to the possibility of a general poisonous effect following their administration by the stomach.

I—THE OXIDE AND CARBONATE OF CALCIUM.

CALCIUM OXIDATUM—CALCARIA USTA.

The calcium oxide, CaO (burnt lime—caustic lime) is made by calcining pure lime carbonate; it is a white amorphous mass, not melted even by the oxihydrogen jet, and converted by the addition of water into calcium hydroxide, much heat being given off during the process.

Physiological action.—The calcium oxide in concentrated solution has a powerful caustic effect upon the skin, similar to that of caustic potash and soda. This caustic action, however, is not so penetrating and spreads less than that of the latter; this is due to the fact that it is not dissolved by the water of the tissue, but changed into calcium hydroxide.

Internally, taken in concentrated solution, it has a burning caustic taste, and a caustic effect upon all of the mucous membranes, so all of the consequences following the administration of the caustic alkalies occur here also, but to a less degree.

The action of the dissolved and diluted caustic lime will be discussed under the head of lime water.

Therapeutic application.—Caustic lime is never used internally, and only as a caustic externally in the same affections in which caustic potash is used. For this purpose, however, it is only used in combination with caustic potash, and not alone.

This combination is in the form of Vienna caustic paste (see caustic potash) and has the effect of somewhat limiting the action, since potash alone used as a caustic is too wide spread in its action; besides this we use caustic lime in varying combinations (with arsenic sulphide, potassium carbonate and sodium sulphide) as a depilatory agent.

AQUA CALCIS—CALCARIA SOLUTA.

The burnt lime CaO, as has been stated, when brought in contact with water is changed into a white amorphous mass, the calcium hydroxide $CaO(OH)_2$; one part of this hydroxide dissolves in 600 parts of cold and 1200 parts of hot water. Such a solution is known as lime water—aqua calcis, this has an alkaline reaction, is as colorless and odorless as ordinary water—but when exposed to the air absorbs carbonic acid, so that the solution becomes cloudy from the formation of lime carbonate, which falls to the bottom as a precipitate.

PHYSIOLOGICAL ACTION.

Internally administered, lime water combines with the acid of the stomach, a small part of the newly formed lime salts is absorbed. The larger part is passed out of the body with the fæces under the same circumstances as the lime carbonate. In passing through the gastro-intestinal canal it diminishes the

glandular secretions of the mucous membranes with which it comes in contact; the causes of this effect are not yet known; but it is owing to this diminution in the quantity of these secretions that the long continued use of this preparation is followed by loss of appetite, nausea and constipation. Inasmuch as it forms insoluble soaps with the fatty acids, it can be utilized in cutaneous and intestinal ulcers, over which the lime water will form a a soap, which will protect the ulcer from the action of the air or intestinal juices, and facilitate the healing process.

THERAPEUTIC APPLICATION.

The most frequent use of lime water is to neutralize acids, under circumstances similar to those in which the lime carbonate is used, as in pyrosis or in diarrhœa (especially of children) which have been produced by acid fermentation of the food. In the latter cases we often add lime water to the milk. It can also be used as an antidote in cases of poisoning by acids, but should be administered in large doses. Lime water has also been used as an astringent in the diarrhœa of adults, when this is kept up by ulcerative process in the intestines. The good effect, which can not be entirely denied, is probably due to the formation of an insoluble compound by the union of the lime water with the secretions of the sore, which protects the sensitive nerves from the action of the intestinal contents. We have, however, better remedies for these cases which are not accompanied by the ill-effects that follow the long continued use of this remedy. As to its application in rickets, compare with what is said under the head of lime carbonate.

Croup membranes easily dissolve in lime water, or according to Bensen, more easily in a mixture of lime water and glycerine. This was first shown by Kuechenmeister, and confirmed by others. Lithium carbonate and lactate alone can in this respect be compared to lime water. Lime water has therefore been given as an inhalation or directly applied with the brush (Gottstein) in diphtheria of the throat and croup of the larynx. Experience, however, has not shown any such results as some physicians originally expected from this method of treatment. The few favorable observations are opposed by so many doubtful and unfavorable ones, our own among the rest, that we do not hesitate to predict that in a few years this method of treatment of diphtheria and croup will be entirely abandoned. Nobody has yet shown that severe cases of diph-

theria have had their course modified by the energetic use of lime water. This method of treatment generally deserts us in extreme cases, while slight cases generally get well under the use of warm water. If inhaled in laryngeal croup it is doubtful whether a sufficient quantity of the lime, to be of any use, ever reaches the larynx, and whether the whole of the lime is not converted into a carbonate long before it reaches the larynx. The use of lime water in a series of other conditions, such as bronchial and vaginal catarrh, diabetes, and uric acid diathesis, is without any effect.

Externally lime water is quite extensively used. In burns of the first and second degrees, in the form of carron oil (linseed oil and lime water). Also used to produce "scabbing" in suppurating wounds, and as a drying application in moist skin affections (eczema, impetigo).

Dosage.—Aqua Calcis, internally in large doses, beginning with 25.0–100.0, several times a day, and sometimes increased to one or two pounds. Taken either pure or with milk, whey or beef soup. Externally as a gargle, etc., either pure or mixed with water.

CALCIUM CARBONICUM—LIME CARBONATE.

The calcium carbonate (CO_3Ca) is one of the most largely distributed minerals (lime, marble, chalk). Insoluble in ordinary water, but soluble in carbonic acid water, from which it is again precipitated when the carbonic acid evaporates. Now we use the chemically pure preparation (c. carbonicum precipitatum); formerly other impure preparations, occurring in nature in combination with organic materials, were used, as for example, chalk (creta preparata), marble, coral, lime shells (ossa sepiæ), muscle shells (conchæ preparata), and cancer stones (lapidis cancrorum).

PHYSIOLOGICAL IMPORTANCE AND ACTION.

The lime carbonate is found as the principal constituent in all of the firm portions of the non-vertebrates (shells of muscles and snails), but in smaller quantity in the bones and teeth of the vertebrates, where the lime phosphate is the predominating component. The only exception to this is in the eggshells of birds and of a few amphibians, in which the carbonate predominates. Pathologically this salt is found in many concretions, such as the salivary concretions and urinary calculi and calcified tubercle.

In a dissolved state it is found in the parotid saliva of the horse and dog, in the urine of the herbivora, but not in that of man.

Internally administered it unites with the acid of the stomach, carbonic acid being given off, is partly absorbed, and changed in the human blood into a phosphate, which accounts for the absence of the carbonate from the urine, while the greater part which is not absorbed, is probably reconverted in the lower portion of the intestinal canal into a simple carbonate. In the herbivora the circumstances must be somewhat different, since in their urine considerable quantities of calcium carbonate are present.

Under any circumstances the carbonate is of very little importance in the physiological economy of man ; it can easily be replaced by the lime phosphate ; so that we shall postpone the consideration of the importance of lime in the body until we come to consider calcium phosphate.

During its passage through the intestinal canal, we observe, as was also the case in lime water, a diminution in the quantity of the secretion, an obstructive action, of which we do not know the direct cause.

THERAPEUTIC APPLICATION.

Calcium carbonate is often used to neutralize acids. In the frequent condition known as pyrosis, which as a rule is the result of an abnormal fermentative process, this salt is used symptomatically, whether this symptom be the result of an anatomical lesion of the stomach or not. Experience has shown that lime has the property of producing slight constipation, even in the healthy state, but certainly of checking a certain form of diarrhœa. Therefore, when compared with the other acid neutralizers, such as sodium, potassium, and magnesium, lime should be used when there is also a tendency to diarrhœa, and avoided where there is a rather constipated condition of the bowels. This preparation should not be given (as was already noted under sod. bicarb.) for too long a time or in too large doses. Furthermore, it is a remedy which is often used in the gastro-enteritis of children, which is caused by an abnormal acid formation (from the milk diet especially), and in which we have dark, sour matter vomited, green colored stools, etc. In this condition, however, aqua calcis is more frequently used (see this preparation). Lime carbonate, in the form of the easily obtained chalk, is a good *antidote against acid poisons.* Lime (in the form of carbonate, phosphate, and lacto-phosphate and lime water) is much given for those conditions of the bones or other tissues in which either an actual or a sup-

posed deficiency of the lime salts exists; that is to say in rickets and osteomalacia. The curability of the latter disease is, as is well known, doubtful. As to rickets, this often gets better without the medicinal administration of lime. The question in this latter case, then, can be only whether the administration of lime, in any practicable dietetic way, is followed by a quickening of the curative process which has already set in. This question has been differently answered by different observers, but evidently the lime salts will be most indicated in those cases of rickets in which we have in addition digestive disturbances demanding their use.

The further application of the remedy in other conditions, as in tuberculosis, has not been borne out by experience. In gout and uric acid diathesis other remedies should certainly be preferred. Only in such cases that have a tendency to diarrhœa might the lime be used from time to time, instead of the alkaline salts. The reported utility of crab and oyster shells (conchæ preparatæ) in "cramps and epilepsy," especially of children, as reported by Hufeland, Goelis and others (from which originates the custom of making these substances a component of antiepileptic and antispasmodic powders) is probably explained by the fact that these convulsions were originally dependent upon a gastro-intestinal catarrh.

Externally lime carbonate is quite frequently used. It forms a component of many tooth powders, rather on account of its mechanical properties than for chemical ones. In ulcers, intertrigo and weeping eczema it is used as a dressing and powder. It is also used in burns, made into a liniment with oil.

Dosage and Preparations.—1. Calcium carbonicum precipitatum 0.5—2.0 per dose (10.0 per day), in powder or in suspension. For cases of poisoning with acids the ordinary chalk may be given in the requisite quantities.

2. Conchæ preparatæ. Prepared oyster shells, a white, fine powder, resembling the foregoing preparation.

3. Mineral waters containing lime. A large number of springs contain lime, either in the form of the sulphate or carbonate. In the large majority of springs we have, in addition, other salts, which are either the chief or at least active ingredients. Such are the sodium carbonate, sodium or magnesium sulphate, sodium chloride, iron and sulphur. In very few springs only are the lime carbonates and sulphates the chief constituents, and these alone are called lime springs.

It is very doubtful, however, whether the lime takes any part in the production of the good effect which these springs exert. We have been pretty well cured of any such delusion. The therapeutic value of these waters rests rather upon the general climatic and dietetic conditions which their systematic use necessitates. To these waters belong: 1. Lipp-springe and the *Inselbad,* near Paderborn, contain small quantities of lime carbonate,

about an equal amount of sodium sulphate, a few other salts, and some nitrogen gas. This spring is chiefly used in phthisis. 2. Weissenburg, in Canton Berne, situated at an elevation. The spring contains principally gypsum. 3. Wildungen, in Waldeck. The George-Victor Spring contains, in addition to a noticeable amount of free carbonic acid, only lime and magnesium bicarbonate; the Helenen Spring contains, in addition, sodium chloride and bicarbonate. The principal indications for the use of these springs are almost exclusively those diseases of the urinary passages mentioned under the head of sodium bicarbonate (lithiasis and catarrhal inflammation of the kidney and bladder). 4. Leuk, in Canton Wallis, contains a large quantity of gypsum. The water (temperature of 50°C.) is used principally for baths in various chronic diseases of the skin; internally it acts only as warm water.

II. THE OXIDE AND THE CARBONIC AND VEGETABLE ACID COMPOUNDS OF MAGNESIUM.

PHYSIOLOGICAL ACTION.

Buchheim and Magawly have stated that most of the magnesium compounds when introduced into the stomach or directly into the intestine are changed to magnesium bicarbonate, and act as cathartics. Salts undergoing such a change are magnesium oxide, carbonate, citrate, tartrate, oxalate, benzoate and chloride.

The lime salts are changed in the intestinal canal into simple carbonates and are therefore without any effect upon the mucous membrane of the intestine, but the magnesium carbonate has an action similar to that of the sodium sulphate. On account of the slight absorption of the former salt, the action of the magnesium cathartic salt is more local than that of the other cathartic salts, and should therefore be preferred.

Where small doses of any of the above salts are administered they are absorbed into the blood in the form of magnesium chloride or lactate, and causing diuresis they soon reappear in the urine. In large cathartic doses however no increase of the urinary excretion is observed.

Husemann believes that the conversion into a bicarbonate is not complete until the salt has reached the lower part of the intestine, and thus explains the delay which occurs before a cathartic effect is produced.

Therapeutic application of the oxide and carbonate of magnesium.—Again we consider the therapeutic indications for the magnesium oxide and carbonate together, as being substantially the same. Both are extensively used as acid neutralizers in those affections of the stomach and intestines, of which a promi-

nent symptom is the formation of acids, as we mentioned when speaking of sodium bicarbonate and aqua calcis. The magnesium preparations, on account of their laxative effect should be preferred to the latter remedies when there is a tendency to constipated bowels. But to produce a cathartic effect somewhat larger doses are necessary. We may on the contrary however administer these salts in the diarrhœa of children, when it is the accompaniment or the consequence of an abnormal acid fermentation in the intestine. The salts have the further advantage over the lime salts in that they do not disturb the digestive functions, even when used for a long time. Whether in these cases we use the oxide or carbonate seems to make no essential difference.

Furthermore, magnesia is a good antidote against poisoning by acids, such as sulphuric, nitric, hydrochloric, acetic and oxalic acids. Magnesia usta has also been proposed in cases of poisoning by corrosive sublimate or copper salts. It is of doubtful utility in poisoning by phosphorus, and is even by some thought to be contra-indicated. It is, on the other hand, one of the best antidotes to arsenical poisoning, even if the magnesium arsenite is not entirely insoluble. As a rule, in cases of poisoning the magnesium should be administered in excess.

In other conditions in which magnesium has been recommended, as in convulsions, uric acid diathesis, etc., it is entirely useless.

MAGNESIUM OXIDATUM—MAGNESIA USTA.

The magnesium oxide MgO (burnt magnesia, talc earth) is a white, amorphous, not meltable powder, which is insoluble in water, but combines with it, giving off heat and forming the magnesium hydroxide $Mg(OH)_2$ (Magnesia hydrat.)

PHYSIOLOGICAL ACTION.

In the stomach this salt is changed into a chloride by the action of the muriatic acid of the gastric juice, and then it undergoes the changes mentioned in the introductory portion to this subject. So that in the stomach it is strongly basic; furthermore it is a diuretic in small doses and cathartic in larger doses.

Inasmuch as magnesia usta when given in sufficient quantity, *renders the contents* of the stomach strongly alkaline, *it is one of the best* means of preventing the absorption of a

number of powerful poisons, such as the metallic oxides, and the alkaloids, all of which are insoluble in alkaline solutions, and therefore can not be absorbed.

Indeed, arsenious acid forms an insoluble salt with the magnesia in alkaline solutions.

Inasmuch as magnesia has considerable absorptive power for carbonic acid (1.0 grm. binds 1100 ccm. of carbonic acid) it would be well fitted to absorb at least a portion of the intestinal gas in meteorism. But unfortunately, owing to the immobility of the enormously tense intestinal wall, the chances of the magnesia passing along the intestinal canal are very slim, and hence this action of the drug is very uncertain (Buchheim).

It is said that the long-continued use of magnesia is followed by the formation of concretions in the large intestine, (perhaps the ammonio-phosphate of magnesia as in the herbivora) which may lead to perforation of the intestine. A woman who died of peritonitis caused by such a concretion, had certainly taken 1–2 teaspoonfuls of magnesia daily for 2½ years. The therapeutic application has already been discussed on page 77.

Dosage and Preparation. 1. Magnesia usta. Is an antacid, from 0.2–1.0 (10.0 per day); should a cathartic effect also be required, we may give 0.5–2.0 in pastilles or in suspension. Its administration in powder is disagreeable because it takes up such a large space and is not easily swallowed. Should be given in large quantities when used as an antidote in cases of poisoning.

2. Trochisci magnesiæ usta, each contains 0.1 of magnesiæ usta.

MAGNESIA CARBONICUM—MAGNESIA ALBA.

By the addition of potassium or sodium carbonate to solutions of magnesium sulphate for example, we have a precipitate formed, which when dried at a low temperature becomes a voluminous white powder which can be represented by the formula $3\ (CO_3\ Mg) + Mg\ (OH_2) + 4H_2O$. This is the magnesia alba of the German pharmacopœia. This is not so insoluble (1–3000 parts of cold, 1–10000 parts of hot water) as the magnesia usta. In water containing a large amount of carbonic acid it is completely dissolved, precipitating after a time in fine needles, the neutral salt $Co_3\ Mg + 3H_2O$. When calcined it is changed into magnesium oxide, carbonic acid and water being liberated.

PHYSIOLOGICAL IMPORTANCE AND ACTION.

Magnesium carbonate occurs in very small quantities in the *bones of the* vertebrates—and as a result in the urine of the *herbivora.* Lehman believes that it is formed in the body by

the decomposition of the magnesium phosphate, inasmuch as magnesium does not occur in cereals and grasses in combination with carbonic or vegetable acids, but is there present as magnesium phosphate.

When the carbonate is introduced into the stomach it has almost the same effect as magnesia usta, and is only distinguished from the latter by the liberation of carbonic acid in the stomach ; in the lower sections of the intestine, they are both changed into magnesium bi-carbonate.

The therapeutic application is discussed on page 77 together with that of the preceding preparations.

The dosage is the same as that of the magnesium oxide.

The lactate, effervescing citrate, tartrate and acetate of magnesia have a similar action.

These preparations are entirely superfluous.

They are mostly administered in larger doses, (point of a knife or teaspoonful), as seldom used cathartics, having a pleasant taste, but being rather expensive.

3.—MAGNESIUM SULPHURICUM—SAL-AMARUM—EPSOM SALTS.

The magnesium sulphate, $Mg\ So_4 + 7\ H_2\ o$ is crystallized from its solution in water at a low temperature, appearing in large, colorless, transparent, rhombic crystals, soluble in four-fifths parts of water at ordinary temperature, and in smaller quantities of hot water.

PHYSIOLOGICAL ACTION.

Bitter salt (Epsom salt) has a peculiar bitter taste, similiar to but pleasanter than that of Glauber's salt (sodium sulphate.) It is also said to be less disturbing to the digestive functions.

The physiological action of this salt upon the intestine is a cathartic effect, depending on causes similar to that of sodium sulphate ; we can therefore refer to what has already been said when discussing the latter salt. It has not the effect of increasing the biliary secretion as sodium sulphate has (Rutherford). It is found unchanged in the fæces.

THERAPEUTIC APPLICATION.

Bitter salt (Epsom salt) is administered under the same circumstances as the sodium sulphate, which have been given in detail under the head of this salt. If we wish to use the pure salt, not as dissolved in mineral waters, we should prefer Epsom salt to *Glauber's salt*, because it is less disturbing to the digestive *functions*.

Dosage.—1. Magnesium sulphur. depuratum (like the sod. sulph.) 15–50 grms.

2. Magnes. sulphur. sicc. in doses half as large.

3. Bitter waters. These contain as a principal constituent magnesium sulphate, and also as a rule Glauber's salt (sometimes in like quantities with magnes. sulph.) and sodium chloride. The indications for their use are essentially the same as those of the so-called alkaline saline springs, with this difference, that the first are exported and taken less at the springs, and also that lately the alkaline saline waters are preferred when they are to be administered for a long time, because these, especially the chief one of them, Karlsbad, produce less disturbances in the digestive functions. Several of the bitter waters, however, can be taken for a long time without harm.

1. Friedrichshall in Saxony, Meiningen—cold—contains, 0.55 % of Epsom salt, 0.6 % Glauber's salt, and about 0.9 % of Na Cl. Very much used. 2. Pullna in Bohemia, 1.2 % of Epsom salt and 1.6 % of Glauber's salt, little sod. chloride. Not well adapted for long continued use. 3. Saidschütz in Bohemia, 1.1 % of Epsom salt, 0.6 % of Glauber's salt. 4. Seidlitz in Bohemia, almost exclusively a bitter salt (Epsom salt) spring, almost, 1.4 %. Stronger still is the lately introduced Hunyadi-Janos spring near Ofen in Hungary, contains 1.6 % Epsom salt, and almost an equal amount of Glauber's salts.

There are many more "bitter springs" as in Kissingen, Rehme, Mergentheim, several in Hungary and Siebenburgen. In England we have Epsom, whence the name Epsom salts for this salt.

4 —COMPOUNDS OF CALCIUM AND MAGNESIUM WITH PHOSPHORIC ACID.

Physiological Importance—The lime and magnesium phosphates are of about equal importance for nutrition. The lime phosphate, however, is found in much larger proportion in the tissues of the body than the corresponding magnesium salt, and for this reason we shall devote more attention to the former salt. Both salts are present in all the animal tissues and fluids partly dissolved, and most probably in combination with an albuminoid, (for alone they would not be soluble in water, and furthermore the neutral lime phosphate is found in the ashes of even the purest albuminoid substances), but to a greater extent they are deposited in the bones and teeth in the form of neutral salt. [$(Po_4)_2$ CO_3]. In 100 parts, by weight, of human bones, we find 57 parts of lime phosphate and only 8 parts of lime carbonate. In the enamel of teeth we have 88 % of the phosphate and only 8 % of the carbonate. We are therefore justified in believing that the earthy phosphates are the chief constituents of the bones, which gives them their hardness. But in the growing cells and in all of growing organs the earthy phosphates seem to form an essential constituent. C. Schmidt found even in non-vertebrate animals, in which the carbonate is the chief mineral substance, that in parts which are rapidly growing, the lime phosphate varies with the intensity of the growing process. He believes that a certain combination of albumen with lime phosphate, possesses the property, when in contact with heterogeneous bodies, of forming a relatively firm membrane around these, that is to say a sort of cell wall. Liebig says that when the blood circulates through the muscular vessels the alkaline phosphate returns to the circulation, while the lime phosphate to a certain extent remains in the cell in a chemical combination.

Both the calcium and magnesium phosphates are introduced into the body

principally with the diet. Animal as well as vegetable food contains a similar proportion of lime, on an average one-thousandth part. In figs and cheese the largest proportion of lime occurs. In animal food the percentage of magnesium is very much lower than that of calcium.

The following is the proportion of lime and magnesia phosphates in the most important articles of diet. Taken from Moleschott's tables.

A.) Vegetable food contains	in	1000	parts
	Ca	Mg	$Po_4 H_3$
Potatoes	0.26	0.53	1.79
Rice	0 35	0.21	3.12
Wheat	0.57	2.21	9.98
Barley	0.65	1.79	11.32
Rye	0.77	1.61	6.56
Peas	1.04	1.82	8.50
Lentils	1.04	0.41	5.97
Asparagus	1.27	0.14	1.13
Carrots	2.33	0.64	2.17
Almonds	4.2	8.42	20.79
Figs	6.48	3.16	0.44
B.) Animal food			
Albumen of egg	0.10	0.10	0.22
Mutton	0.13	0.15	3.73
Beef	0.51	0.23	4.35
Pork	0.83	0.54	4.94
Yolk of egg	1.63	0.26	6.57
Cheese	5.23	0.20	9.06

We can thus easily determine that the ordinary diet is fully capable of supplying all of the earthy phosphates necessary to make up for the daily loss, which is one gram in adults. Besides this it has been positively determined that the earthy phosphates are formed by decomposition in the body (alimentary canal and blood) of the earthy carbonates and alkaline phosphates. It is also possible (Diaconou) that the lime phosphate found in the fœtus owes its origin partly to the lecithin, which is decomposed in moist air into phosphoric acid, glycerophosphoric acid being also formed, and which in the yolk of egg is accompanied by a combination of lime, which is soluble in alcohol and ether. Unhatched eggs contain a smaller percentage of lime phosphate than eggs that have been long in the process of hatching, or the newly hatched chick. Young bones also are richer in lime carbonate which is changed into phosphate later on. Notwithstanding this, it is possible that the disturbances in nutrition which result from an exclusive potato diet, are due in part to the small percentage of earthy phosphate contained in such a diet (Beneke), although experiments upon pigs have shown that such a want of earthy phosphate is replaced plentifully by the amount of these salts taken in the drink (Boussingault).

Just as the alkalies are changed, when introduced into the stomach, so the earthy phosphates undergo a change when brought in contact with the gastric juice ; calcium chloride is probably formed, while phosphoric acid and acid phosphates occur free in the chyle. These are partly absorbed into the blood and partly changed into basic salts in the intestine.

There *is not the slightest* doubt of the daily absorption into the blood of *small amounts of earthy phosphates*. The intestinal mucous membrane of

herbivora and birds is best fitted for the absorbtion of lime and magnesium salts. A cock can absorb more calcium in one day than an adult person. In the carnivora and in man much less earthy phosphates are absorbed. Koerber found that with a similar diet (milk and bread) a one kilogram rabbit excretes in the urine 11 times as much phosphate, (12 times as much Ca, and 10 times as much Mg) as a dog of one kilogram, although the absolute quantity of urine in both animals was about equal. In the carnivora the largest part is excreted with the fæces unchanged or turned into carbonate, while on the other hand earthy salts which have been absorbed into the blood are not again excreted through the intestine, but reappear in the urine; as Koerber has shown for magnesium sulphate injected into the blood.

With marvelous unanimity almost all observers found that a healthy adult man excretes in the urine one-third gram of earthy phosphates per day. The daily amount of calcium phosphate amounts on an average to 0.31–0.37 grms. (0.005 per kilo. of bodily weight); of magnesium phosphate the average amount is 0.64 grm. It 100 parts, then, we have 33 parts of lime phosphate, 67 parts of magnesium phosphate, (Neubauer and Vogel). The acid reaction of the normal human urine is dependent upon the acid phosphates.

Hirschberg found in old people a smaller amount of lime excreted during the 24 hours than in young people, while a relatively larger amount was found excreted by rachitic children.

When large amounts of earthy phosphates are introduced into the stomach, we find, in the herbivora, a correspondingly larger amount absorbed and excreted in the urine; as to the carnivora and man, we have a number of contradictory observations, which we shall give in full because of the importance of accurate knowledge upon this point in the treatment of rickets. The weight of evidence, however, seems to incline in favor of the theory, that in carnivora and men also, there is an increased absorbtion of the salt with increased supply.

Buchheim–Koerber added to the diet of dogs and rabbits, (this diet consisting of bread and milk given in like quantities to both animals,) an amount of earthy phosphates, administering it to dogs in the shape of bone, to rabbits as the pure salt. They found that while in the rabbit a larger quantity of phosphates were absorbed, and excreted in the urine, an entirely different result was seen in the carnivora, for here the increased supply of phosphates was without effect, being excreted, unused, with the fæces and hindering even the physiological absorption of earthy phosphates from the food. It might be objected, however, that the phosphates administered to dogs in the shape of bone, were less favorable to absorption than the pure salt given to the rabbit.

Neubauer administered to four young men, in whose urine he had first accurately determined the normal amount of lime excreted, 1 grm. of various lime salts at bed time, and obtained the following result:

1. Subject for experiment had normally in the urine of Ca........0.303
   after 1 gram. of CaCl..........................0.397
2. " " experiment had normally in the urine of Ca........0.267
   after 1 gram $CaOCO_2$..........................0.310
3. " " experiment had normally in the urine of Ca........0.282
   after 1 gram CaOA..........................0.324
4. " " experiment had normally in the urine of Ca........0.387
   after 1 gram 3 $CaOPO_5$..........................0.489

We thus clearly see in all four of the cases an increase, however small, in *the amount of* calcium excreted.

Riessel, whose experiments, made under the guidance of Hoppe-Seyler, are of interest also in reference to the change of the carbonates into phosphates while passing through the organism, started out with the view that the administration of lime carbonate would after a time effect an entire removal of phosphoric acid from the urine, but reached entirely different conclusions. Although in the beginning when large quantities of lime carbonate were taken (10.0 grms. at every meal) it was indeed true, that the excretion of phosphoric acid by the urine was diminished, yet later on the amount again rose to the normal. But the normal relation of the alkaline and earthy phosphates were reversed. In the normal condition before the administration of chalk, the phosphoric acid was chiefly united with the alkalies; after the administration of chalk, however, the amount of alkalies excreted became much smaller, and the whole of the increase was combined with earths, and principally with lime. Riessel therefore concluded (and this conclusion was warranted by further observation) that the lime phosphate was absorbed with difficulty on account of its difficult solubility, and therefore, when large quantities of this salt were formed, only a small portion was absorbed, while a much larger portion was excreted by the fæces; but that the continual presence of considerable quantities of this salt (which must have been formed in his experiments from the decomposition of the carbonate) overcame the difficulties to absorption, and thus larger amounts of lime phosphate were taken up, and again excreted through the urine.

Soborow also found, in his observations, made upon young men and dogs, an increased excretion in the urine, with an increased supply of chalk.

Furthermore Lehman had already found, that under an ordinary diet 1.09 grms. of earthy phosphates were excreted with the urine in 24 hours, while under a meat diet 3.56 grms. were excreted.

Zalesky experimented, under the direction of Hoppe-Seyler, upon young doves. To a number of these he gave an additional amount of lime, to others phosphoric acid without lime (sodium phosphate) besides the ordinary food, and observed these birds for 103 days. They remained lively and healthy; the bodily weight and fat were increased. Finally the birds were intentionally killed, and the most accurate analysis of the bones showed no difference. Zalesky therefore concludes that the addition of lime or phosphoric acid to the food has no influence either upon the relation of the organic to the inorganic constituents of the bones, or of the lime to the phosphoric acid.

But there is still a lack of accurate comparative observations in which the earthy phosphates absorbed and those excreted with the fæces and urine would be quantitively determined. And the assertion of many physicians and experimenters, that fractures of the bones in men and guinea pigs heal more rapidly and with a firmer callus under an increased supply of lime phosphate, certainly needs more convincing proofs.

Magnesium phosphate is found in the excrement of the herbivora in larger quantities than the lime phosphate, and is also present in the excrement of the purely carnivorous animals. For this reason it was concluded that the mucous membrane of the intestine has a greater absorption power for calcium than for magnesium phosphate. But we find in the urine equally large quantities of magnesium phosphate, therefore the above surplus can be better explained by the theory that the magnesium phosphate is inclined to form with the ammonia of the intestinal contents an almost insoluble crystalline salt, the *magnesium-ammonium* phosphate ($PO_4MgNH_4 + 6H_2O$), *of which, indeed, the* larger part of the intestinal concretions found in *herbivora consists (Lehman).*

Clear and convincing as are the known facts concerning the importance of the earthy phosphates for general nutrition and especially for the growth of bones, yet equally contradictory are the results of experiments concerning the effect of the withdrawal of the earthy phosphates from the food. Theoretically the matter appeared very simple, since it was known that in some diseases of the bones, rachitis, and osteomalacia, a considerable diminution of the normal percentage of lime phosphate in the bones could be shown. (According to Valentine a healthy human bone has 84%, a carious one 77% of lime phosphate. According to Davis a healthy bone 66% of inorganic constituents, while a pathological bone has only 16% of lime phosphates and 4% of magnesium phosphate and lime carbonate.) So that it was concluded that the cause of these diseases was a diminished supply of lime phosphate (rickets) or too great a waste of these salts (osteomalacia), this being further believed to be proved by the facts that in children rickets most often occurs where large quantities of lime phosphate are needed for the growth of the teeth, while osteomalacia most often affects pregnant women, in whom quantities of lime phosphate are needed for the formation of the bones of the fœtus.

But since it was frequently observed that these diseases continued, even under an increased supply of lime phosphate, it was necessary to form some other hypothesis, and it was supposed that there existed in these cases either an increased difficulty of absorption of lime phosphate by the mucous membrane, or an increase in the organic acids (lactic and oxalic acids) of the organisms by which the lime was dissolved out of the bones. For none of these theories, however, have we any proof. The assertion that lactic or other acids, by a simple solution of the lime phosphate, could give rise to rachitis or osteomalacia, may be considered as unproved, or even as refuted. For anatomical observation of the diseased bones has taught us that the disease does not depend upon a simple withdrawal of the phosphatic salts, but upon a pathological change in the organized base of the bones. Furthermore it has never been proved in a satisfactory manner that in these diseases of the bones a greater amount of earthy phosphates were excreted in the urine and fæces than were introduced in the food or than healthy persons excreted under a like diet. We may also be sure that the acids found in the urine, which the older observers considered lactic acid, were nothing else than phosphoric acid. Furthermore the marrow that can be poured out of a bone affected by osteomalacia has not an acid but an alkaline reaction. And finally the assertion of Heitzmann, that rachitis could be produced in animals by lactic acid injections has been well disproved by Heiss. As to the experiments in which the earthy phosphates were withdrawn from the diet of animals, we have contradictory results obtained by different observers, and inasmuch as it is impossible to arrive at any positive conclusion at present, we will briefly again recount these observations, passing over such only as are too long or which contain errors which have been already disproved, as for instance the observations of Mouries, who pretends that in a healthy woman the enormous quantity of 5.0 grms. of lime phosphate was excreted by the urine and 1 grm. worn off with the epithelium (nails and hair), and compares with this quantity as a normal standard, a series of observations obtained in diseased conditions, with the object of demonstrating a connection between the bodily temperature and the amount of lime contained in the body.

Chossat observed, after depriving pigeons for a long time of lime salts, that friability of the bones and diarrhœa set in, but could not decide whether this was due to the reabsorption of the lime salts only or of the

whole of the base of the *bone*. Dusard found in a pigeon, that after an insufficient supply of lime, the proportion of lime in the body was diminished; with a daily absorption of only 0.039 grm., there was a daily excretion of 0.098 grm. Roloff in Halle communicated observations upon cows, which were fed upon hay poor in lime and phosphoric acid, and as a consequence suffered from serious disturbances of digestion and friability of the bones: when these, after the lapse of a year, were again fed upon hay which was richer in the above constituents, they recovered after four weeks of this improved diet, so that they were able to run around in a lively manner upon the pasture, whereas formerly they had been scarcely able to place one foot before the other. But since, in this neighborhood, cows became rachitic even when fed with an additional quantity of phosphoric acid, Roloff supposes (positive observations are wanting in the entire matter), that it was not the lack of phosphoric acid but the lack of lime that caused the rachitis. The fact that cows, pastured upon an earth rich in lime are also affected with rickets, proves nothing, since he had examined hay grown on earth rich in lime, and found that, notwithstanding, it contained only of lime (0.56%) and phosphoric acid (0.18%.) Milne-Edwards fed young, not full grown, pigeons upon a diet very poor in lime. They became affected with diarrhœa after three months, were very miserable, and soon died. Their bones had a much smaller volume than usual, and weighed at least ⅓ less than the birds that had been fed on healthy diet. *The composition of the bones themselves however was not altered.* Weiske and Wildt reached the following conclusions: 1. The withdrawal of lime and phosphoric acid from the food of grown animals (goats) led, it is true, to disadvantageous results, such as wasting and finally death, but did not produce any effect upon the composition of the bones, nor any friability of these. The observed increase then in the amount of phosphoric acid excreted as compared with that taken in, must be presumed to have been supplied by the softer tissues of the animal while the phosphoric acid of the bones combined with mineral substances remained behind as a firm constituent. 2. In young growing animals the composition of the bones is not altered in any noteworthy manner, by the abstraction of lime or phosphoric acid from the food. The bones indeed do not develop to as great an extent as under the normally rich diet, but no chemical or physical change (bone disease) is produced in the bones. 3. Various amounts of earthy phosphates added to the diet of animals (rabbits) of different ages do not influence the composition of the bones.

We can not help seeing then that out of the above observations the most trustworthy, those of Milne-Edwards and Weiske, do not speak in favor of the theory that bone diseases are caused by the withdrawal of lime phosphate from the food, but simply that such withdrawal produces a disturbance in nutrition, and in consequence of this, death.

CALCIUM PHOSPHORICUM—LIME PHOSPHATE.

There are three compounds of phosphoric acid with calcium.

1. Neutral $(PO_4)_2\,Ca_3$. 2. Simple acid, $PO_4\,HCa+2H_2\,O$, and 3. The double acid $(PO_4\,H_2)_2\,Ca+H_2O$ lime phosphate. To which of these three compounds that ordered by the German pharmacopœia belongs is not known; it is probably however the neutral salt. It is to be precipitated *from a solution of 20 parts* of lime carbonate to 50 parts each of water and *hydrochloric acid, by* the addition of a solution of sodium phosphate of the

strength of 50 to 300. It is a light, white powder, insoluble in water, but slightly soluble in carbonic acid water.

Physiological Action.—Lime phosphate when introduced into the stomach is absorbed in the manner stated above. The larger part of large doses is passed out of the body with the fæces. The only phenomenon observed after the use of large quantities is the extreme dryness of the fæces (s for instance, the white fæces of dogs fed upon bones).

Therapeutic Application. Upon theoretical grounds, the lime phosphate has again lately been recommended in diseases of the osseous systems and especially in rickets. Experience however does not bear out the theoretical indications, for we have never seen a case of rickets cured only by the medicinal administration of lime phosphate; while on the other hand daily observation teaches that rachitis is cured by the fulfillment of other well known dietetic and hygienic conditions, without a centigram of lime phosphate being prescribed from the druggist. Probably the organism received the necessary amount of lime with the diet, after the affection of the intestine that hinders the absorption, or other anomalies of tissue metamorphosis, are cured. What we have just said is true, even to a greater extent of osteomalacia. Never, as far as we know, has a case of this disease been cured by the administration of lime. That in healthy individuals the plentiful introduction of lime facilitates the formation of callus in fractures, is yet to be confirmed by a more extended experience. This remedy is also recommended in scrofulous affections, in caries, and in extensively suppurating wounds; but everywhere there is a lack of trustworthy and extensive observations. Clarus recommends the combination of iron and lime phosphate in anæmia.

One advantage which this drug possesses is that it can be used for a long time in quite large quanties without disagreeable results of any kind following, especially if it be given in practicable combinations with bitter and aromatic remedies.

Dosage.—Calcium phosphoricum, 0.5–2.0 several times a day in powder. For children as much as will go upon the point of a knife is mingled with the food.

Appendix to the Alkaline Earths.

The barium compounds are no longer used therapeutically. Their toxicological importance has been considered on pages 83 and 84 in the introduction to the alkaline earths.

The German pharmacopœia still presents the lime sulphate (calcaria sulphurica nata—gypsum ustum) as an officinal remedy, although it is only used for plaster of Paris bandages.

THE AMMONIA COMPOUNDS.

It is generally considered that in the ammonia salts there exists a monatomic compound NH_4 which cannot be isolated, and which plays the part of a compound radical, acting just as a metal; this group of atoms is called ammonium, and is capable of forming with mercury an ammonium-amalgam. It *has, however, not* yet been possible to isolate ammonium, since *it immediately* resolves itself into ammonia NH_3 and H.

This ammonia, which is also produced by the decomposition of nitrogenous organic matters (flesh, blood and urine), acts as a strong base and combines with all of the acids to form ammonium salts, which resemble the potassium salts very much ; they differ from these, however, in volatility (volatile-alkali) and in possessing weaker basic properties.

For this and the further reason that the ammonium salts have a local physiological effect very similar to that of the corresponding alkaline salts (such as caustic action, etc.,) we consider them immediately after the latter.

PHYSIOLOGICAL EFFECTS COMMON TO ALL OF THE AMMONIA COMPOUNDS.

Ammonia is present in the normal organism, in the intestines for example, as the ammonio-magnesium phosphate ; it is also present in the blood and tissues, being partly absorbed from the intestines, and partly set free by the decomposition of the albuminoids (Walter). We can, therefore, in the carnivora at least, distinguish for it two functions ; a neutralizing one, that is to say the function of combining with acids introduced from without (as for example, animal food which according to Hallevorden, should be considered as acid), and thus preserving the fixed alkalies which are necessary to the organism from being used up for this purpose ; and secondly its importance in the formation of urea, of which we shall speak later on. (Pages 105 and 106).

All of the ammonium compounds introduced from without and the ammonia itself, have a similar action, (ammonium action) varying only in intensity. The looser the ammonia combination the stronger is the action of the salt. The weakest of all is the sulphate, next in order the carbonate, then the ammonium chloride and ammonia (Lange).

The local effects also vary with the volatility of the different preparations, that is to say, with the permanence of the ammonia compound. The volatile compounds, as a rule, have the painfully sharp ammonia odor ; can be absorbed into the blood through the skin, as well as by the mucous membrane, and have an irritant action upon the skin and mucous membranes, which is not so strong as that of the alkalies, and due partly to the withdrawal of water from the tissues. The non-volatile ammonia compounds, however, are absorbed only through the mucous membranes.

The *following are the* physiological effects, common to all *of the preparations*, as they have been studied by Lange-Bœhm

and Funke-Deahna. We shall note the difference under the head of each preparation :—

Nervous centers.—In frogs the introduction of ammonia, in whatever manner it may be (whether any of its salts be introduced into the stomach, hypodermically, directly into the blood or by inhalation) produces a great increase in the reflex irritability and also tetanoid convulsions, even after the animal has been decapitated. And finally general paralysis due to exhaustion.

In rabbits, dogs and cats, subcutaneous injection is followed by an increase in the reflex irritability; direct injection into the blood, by tetanus and opisthotonos, due to an increased irritability of those ganglia in the spinal cord, from which the motor tracts of the voluntary muscles originate. After section of the nerves at one hip, the corresponding leg does not show tetanoid convulsions after general ammonia poisoning, but only weak fibrillary contractions. The effect upon the spinal cord is therefore very analagous to the action of strychnia; with this difference, that after the first tetanoid convulsions, every new irritation of the sensitive nerves is not again followed by tetanus, but only by a short reflex contraction, probably because the peripheral nerves have their irritability more rapidly destroyed by ammonia than by strychnia.

In human beings, in whom this drug is introduced naturally by the mouth or by inhalation, very inaccurate observations seem to have shown, that small medicinal doses are followed by hyperæsthesia, trembling and weakness of the limbs (Rabuteau). Wibmer observed upon himself that "ammonia affected the head." Pareira's statement that it produces an increased muscular power and endurance, seems to have originated in theory only, for we have been unable to find any actual ground for such a belief. Even in the reports of cases of fatal poisoning we cannot find any description of convulsions that might be considered as the result of the irritability of the nervous centers.

In the beginning the aspect which the poisoned patient presents is a confused one, on account of the terrible pain produced by swallowing the caustic preparation, or on account of the severe disturbances in respiration; toward the end there is a severe collapse, the patient is pale and unconscious. Only in children in whom ammonia has been injected subcutaneously, have severe convulsions been noticed before death takes place. We, therefore, believe that the nervous centers, in man, are *not excited* by the ordinary small doses administered internally; *and that in* cases where ammonia has been directly inhaled or

administered in large and dangerous doses the nervous centers are excited not by the drug itself but by the painful sensation or the dyspnœa that has been caused by it; and, furthermore, that only the rapid injection of the drug into the blood, or enormously fatal doses, have a direct, at first irritant, then a paralytic effect upon the functions of the spinal cord and brain, somewhat similar to that produced upon animals. Even in fatal poisoning consciousness and the sensation of pain are long retained and do not disappear until shortly before death in consequence of secondary alterations, as, for example, carbonic acid intoxication due to the dyspnœa which is the result of the inhalation of ammonia vapor.

Peripheral nerves and striped muscular fiber. Ammonia is one of the chemical muscle irritants; it produces a rapid chemical change in the composition of the muscle and produces at the point of application a muscular contraction accompanied by muscular rigidity. Contractions occur when only traces of ammonia are mingled with the air in which the cut out muscle lies.

To produce muscular contractions by means of ammonia through the motor nerves, however, much stronger solutions are necessary.

In the living cold-blooded animals injections of ammonia are followed by fibrillary contractions in the muscles, which have had their connection with the spinal cord interrupted and which cannot therefore be affected by any tetanoid condition. Orfila found that in a dog, whom he had killed in 10 minutes by the injection of a solution of caustic ammonia into the jugular vein (the dog dying in convulsions), the muscular contractility was entirely abolished after death.

It is not at all probable that in man any noteworthy alterations in the muscles and peripheral nerves is produced by medicinal doses of this drug.

Respiration.—The more local effect of the volatile ammonia compounds upon respiration we shall consider under the head of ammonia (page 93). Here we only give a general picture of the effect of the introduction of ammonia salts into the blood. When dilute solutions of ammonia or an ammonia salt are injected into the blood of animals, a short interruption, followed by an extraordinary quickening of the respiratory movements is the result, this being due to an irritation of the respiratory center in the medulla oblongata. In animals in which, after such an injection of the ammonia, both vagi are divided, the *operation is no longer* followed by the usual diminishing effect

upon the number of respirations, but these remain increased almost up to death. When both vagi are severed before the poison is injected, the above stated primary interruption does not occur. Both of these latter observations Funke could not confirm by the direct injection of ammonia solutions into the blood.

During the tetanoid state produced by ammonia, the respiratory movement naturally ceases entirely.

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Secretory and excretory organs.—The secretion of many glands, especially of the bronchial glands, and according to some of the sweat glands, is increased by the action of ammonia and various ammonia salts; the mucus of the bronchi also becomes more fluid.

The excretion of urine is also increased, and, while as we have already shown the urine of the carnivora rapidly becomes alkaline after the use of the carbonates and vegetable acid salts of the fixed alkalies, the urine remains acid after the introduction of the corresponding ammonia salts, even when administered in considerable quantities (Schmiedeberg.)

The small though not the large intestine is said to be specifically influenced by the endermatic introduction of the ammonium preparations; an increased separation and solution of the epithelium together with an increased formation of mucus takes place (Mitscherlich.) With the internal administration of ammonium carbonicum pyro-oleosum in horses and cows the food is better digested, and the fæces are in smaller and harder lumps (Hertwig.)

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It is therefore very probable that the volatile alkali introduced into the living blood, is changed into a non-volatile compound; for it can no longer be replaced by hydrogen at the ordinary temperature of the body; in the blood of the dead body such a process does not take place. It is a striking fact that the blood which has been let out of the body of the normal animal gives off ammonia vapors sooner and at lower temperatures, than the blood of animals which were poisoned during life with large quantities of ammonia salts. The ammonia reaction of living blood is not seen until some time has elapsed, and then only at a temperature at which ammonia might have been formed by the decomposition of the normal ingredients of the blood. The blood itself undergoes evident changes only upon the addition of large quantities of ammonia; these changes are, difficulty in coagulating, disappearance of the oxygen spectrum, dissolution of the red blood corpuscles, and destruction of the hæmoglobin. When animals are permitted to inhale large quantities of ammonia, their blood becomes dark in color, but is soon turned red again by the addition of oxygen, and shows the same absorption bands as normal blood.

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toms are produced by the tracheal inspiration of chloroform and other volatile matters. If strong concentrated ammonia be inspired in the same manner, the inspiratory movements become deeper and slower, and an "expiratory tetanus" is produced, due to irritation of the expiratory filaments of the vagus; immediately after this effect, a change of the above relation occurs, the respiration is more shallow and quickened, owing to irritation of the inspiratory filaments of the vagus.

There are cases recorded where people have been suffocated by the inhalation of ammonia. During and after the inhalation the most severe pains in the breast and neck occur, and very painful "coughing" attacks last for a long time. In consequence of the severe bronchitis, the trachea and bronchi are filled with large collections of mucus, and even pneumonia and congestion of the lungs have been known to follow such treatment.

Applied directly and in concentrated form upon the mucous membrane of the larynx, it produces an inflammatory exudation, similar to the naked eye, to croupous membrane.

The general symptoms are not in most cases directly due to the action of the poison, but to local disturbances (gastro-enteritis), and also dependent upon carbonic acid poisoning, etc. The symptoms produced by the poison itself have been thoroughly considered in the introduction.

THERAPEUTIC APPLICATION.

Formerly ammonia gas was given in a variety of pathological conditions, but since it has not shown itself to be of utility in any one of them, we do not consider it necessary, even to give them mention. Only a few conditions in which the remedy has gained a considerable reputation need attention.

Ammonia is at present and has been for a long time past, the most common antidote to the *bites of reptiles*, not only of the vipera berus with us, but also of crotalus horridus, cobra di capello, naja, etc., in short, all poisonous snakes. Many of the results of experiment and practical experience here contradict each other. But since favorable cases are constantly reported, and especially since we have no better remedy, we should always try ammonia in any particular case, together with any other technical means that may be offered. Liquor ammon. caust. 30 drops, diluted with equal parts or 1 : 4 of water may be injected subcutaneously, while at the same time it is administered by the mouth in water. The injection should

be repeated when the serious nervous symptoms again set in. The utility of this drug, applied locally and internally, after the bites of other poisonous animals is well established. It is used in the bites of scolopendrina, spiders, scorpions, hymenoptera and diptera. The recommendation of ammonia used hyperdermatically, by inhalation or by the mouth, in cases of poisoning due to hydrocyanic acid and chlorine, is not supported by practical experience. As an antidote to mineral acid poisons, the remedy is useless, and if given in overdoses might itself do harm. The taking of a few drops of ammonia solution (in much water) is recommended for severe alcoholic intoxication, which is said to be diminished in intensity after the use of this remedy. (Stillè *et al.*) Since it can do no harm in such doses it may be tried, but that it does not alleviate the disagreeable after effects of intoxication by alcohol, for which purpose it is sometimes administered, we can confirm.

Externally ammonia is much more used ; and although, in most cases, other remedies may be substituted for it, so that its use is a matter of individual preference, yet its utility can not be questioned. Ammonia in the form of any of its preparations is applied, as a rule, when a *slightly irritant effect upon the skin* is desired, and when such an effect is to be continued for some time, as in slight chronic articular rheumatism, in chillblains, contusions of the joints, etc. The ammonia preparations belong to a class with which the laity do considerable harm. As a caustic, ammonia is, with propriety, not much used, and for the production of blisters the cantharides preparations are more used.

Ammonia is used for smelling, to produce a strongly irritant effect upon the mucous membrane of the nose (trigeminus) and thus, in a reflex manner influence the respiration ; so used in syncope, severe alcoholic intoxication, narcotic poisons, especially when, in a state of coma, the respiration becomes weaker, and is in danger of entirely ceasing. But the inhalation must be carefully conducted, since, if continued too long, it may produce a spasm of the glottis, which might be followed by serious consequences. In poisoning by carbonic oxide and dioxide, experience shows the inhalation of pure air to be of greater utility than ammonia.

Dosage and Preparations.—1. Liquor ammon. caustici, internally 0.1–0.5 (2–10 drops) greatly diluted with water, administered in mucilaginous vehicles. In snake poisons it should be given in the quantities above indicated. Externally it is applied pure to wounds caused by snakes and insects. As ordinary cutaneous irritant, it is rarely used pure or diluted, but generally i-

the form of one of the officinal preparations given below. For smelling, the ordinary liquor. ammon. caust. is used.

2. Linimentum ammoniatum s. volatile—volatile liniment. 4 parts of ol. olivæ provinc. 1 part of liq. ammon. caust. A white semi-fluid mass, used only as an irritant to skin, externally.

3. Linimentum ammoniato-camphoratum —volatile camphor liniment. 4 of ol. camphorat and 1 of liq. ammon. caust., used like No. 2.

4. Linimentum saponato ammoniatum. Volatile soap liniment. 1 part of common soap, 30 water and 10 of alcohol, 15 of liq. ammon. caust. Use like No. 2.

5. Linimentum saponato-camphoratum, opodeloc. 16 parts of domestic soap, 8 of oil soap, 8 of camphor, 320 of alcohol, 1 of oil of thyme, 1 of oil of rosemary and 16 of liq. ammon. caust. Externally very much used ; as a domestic remedy often misapplied.

6. Linimentum saponato—camphoratum liquidum.—Fluid opodeloc. 30 parts of oil soap, 230 of alcohol, 5 of camphor, 1 part of oil of thyme, 2 of oil of rosemary, 8 of liq. ammon. caust. Used like No. 5.

7. Liq. ammonii caustici spirituosus—spiritus ammon. caustici Dzondii : 10 per cent. solution of ammonia gas—external.

Of the foregoing preparations the last five could easily be spared.

8. Liquor ammonii anisatus, 1 part of oil of anise, 24 of alcohol and 5 of liq. ammon caust. 0.25-0.5 per dose (3-10 drops) given, either alone in a mucilaginous vehicle, for, on account of its irritating effect it produces a cough, or given in combination with other drugs. Therapeutically it is used principally as an expectorant for those conditions which will be more completely enumerated under the head of Senega, but generally where the bronchial secretion is loose and plentiful, but when, owing to a lack of strength, it can not be expectorated. This preparation is often given in combination with senega, but since it is even more irritant than the latter, it must be avoided in acute inflammatory and febrile processes. In other conditions in which this drug may be given, such as meteorism, etc., it is only of secondary importance.

2.—AMMONIUM CHLORIDUM—AMMONIUM CHLORIDE—SAL AMMONIAC.

Ammonium chloride (sal ammoniac) is produced by the union of equal volumes of ammonia and hydrochloric acid gas. It is a white crystalline powder, permanent in air, but volatilized by heat, without melting, thus being to a great extent decomposed into ammonia and hydrochloric acid. Soluble in 2½ parts of cold water and insoluble in absolute alcohol.

PHYSIOLOGICAL ACTION.

Sal ammoniac has a much milder local effect, and is much more poisonous when injected into the blood, than ammonia and carbonate of ammonia. It is fatal, however, from the same causes, in certain doses, and we can, therefore, refer to the general action of these preparations, which have already been described, to facilitate the understanding of its effect.* Men, as well as beasts, die with the development of gastric

* See page 101 and following.

symptoms, increased blood pressure, conditions of psychical disturbances, tetanoid convulsions and finally loss of consciousness, and sensation.

As regards its use in smaller medicinal doses in men and animals, we must next mention its sharply saline and disagreeable taste. The sensation of smell is not affected, since the ammonia molecule is too firmly bound and is not liberated at ordinary temperatures.

Wibmer, who took 0.5–1.2 grms. of sal ammoniac at a time and repeated the dose hourly, reports that the following effects have been observed by him :. A feeling of warmth and uneasiness in the stomach, temporary headache and increased desire for micturition, slight increase in the amount of urine and sweat excreted. Long continued use was apt to cause digestive disturbances, but scarcely ever diarrhœa. Considerable wasting of the body, however, almost always resulted. The most noteworthy effect was that produced by these small doses upon the mucous membranes, especially of the air passages, in which after long-continued use there was even a "phthisis mucosa" established.

Of all of these superficially observed effects, that upon the secretion of mucus has been confirmed by all other observers; it seems, therefore, to be well founded, and to depend upon an action similar to that exerted by sodium chloride, although sal ammoniac has not been shown to appear in the excreted mucus, as sodium chloride has.

Mitscherlich, who observed the mucous secretions of the stomach and intestines in rabbits that were fed with sal ammoniac, and found that they were increased in quantity, saw that the epithelium was softer and composed of fewer large cells; the swollen cylindrical cells, separated from each other with the slightest motion and became admixed with the mucus in large numbers, and were soon dissolved in it.

Furthermore, the increase in the excretion of the urine seems to be a constant effect of sal ammoniac administered internally. Boecker always found in experiments upon himself that he excreted from 250–600 grms. more under these circumstances.

For a time it was believed that the ammonia of sal ammoniac was changed into urea in the body of the rabbit, but not at all or only to the least extent in the dog. (Knieriem, Schmiedeberg.) The latest observations of Munk–Salkowski have shown, however, that even in the latter animals more than 50 % of the sal ammoniac introduced undergoes this change.

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The changes produced upon the human circulation by the internal administration of medicinal and poisonous doses have not yet been observed.

Secretory and excretory organs.—The secretion of many glands, especially of the bronchial glands, and according to some of the sweat glands, is increased by the action of ammonia and various ammonia salts; the mucus of the bronchi also becomes more fluid.

The excretion of urine is also increased, and, while as we have already shown the urine of the carnivora rapidly becomes alkaline after the use of the carbonates and vegetable acid salts of the fixed alkalies, the urine remains acid after the introduction of the corresponding ammonia salts, even when administered in considerable quantities (Schmiedeberg.)

The small though not the large intestine is said to be specifically influenced by the endermatic introduction of the ammonium preparations; an increased separation and solution of the epithelium together with an increased formation of mucus takes place (Mitscherlich.) With the internal administration of ammonium carbonicum pyro-oleosum in horses and cows the food is better digested, and the fæces are in smaller and harder lumps (Hertwig.)

Occurrence in the blood and the excretions.—After it has been believed for a long time that the presence of ammonia can be demonstrated in the expired air of healthy animals and men, it now appears, from the faultless observations of Voit and Bachl, Schiffer, Boehm and Lange, that this is undoubtedly not the case. Even after the injection of the ammonia salts, as for example the carbonate of ammonia, directly into the blood, ammonia could not be shown to be present in the expired air. Even its excretion with the sweat is not probable; when traces of ammonia were found, as in the axillary space and on the feet, it was probably produced by a decomposition of the dead epithelium and dirt.

It is therefore very probable that the volatile alkali introduced into the living blood, is changed into a non-volatile compound; for it can no longer be replaced by hydrogen at the ordinary temperature of the body; in the blood of the dead body such a process does not take place. It is a striking fact that the blood which has been let out of the body of the normal animal gives off ammonia vapors sooner and at lower temperatures, than the blood of animals which were poisoned during life with large quantities of ammonia salts. The ammonia reaction of living blood is not seen until some time has elapsed, and then only at a temperature at which ammonia might have been formed by the decomposition of the normal ingredients of the blood. The blood itself undergoes evident changes only upon the addition of large quantities of ammonia; these changes are, difficulty in coagulating, disappearance of the oxygen spectrum, dissolution of the red blood corpuscles, and destruction of the hæmoglobin. When animals are permitted to inhale large quantities of ammonia, their blood becomes dark in color, but is soon turned red again by the addition of oxygen, and shows the same absorption bands as normal blood.

Neubauer and Buchheim-Lohrer believe that in the urine of men and animals at least a portion of the absorbed ammonia can again be found. But on the other hand Shiffer (accord-

ing to Salkowski), after the injection of ammonium carbonate, searched in vain for its presence in the urine (dogs and rabbits). Now it has been firmly established by the investigations of Gaehtgens-Knierim, Salkowski, Schmiedeberg and Hallervorden, that ammonia and a large part of its salts, as for example ammonium carbonate, are changed, by synthesis, into urea in the bodies of the herbivora and carnivora, and appear as such in the urine ; and that this is the reason why former investigators failed to find in the expired air or in the urine the ammonia as such.

Schmiedeberg believes it probable, that all of the nitrogen compounds, in which nitrogen is present in the form of NH_2—CH_2—are decomposed in the organism into ammonia, and that the carbonate of the latter is immediately changed into urea by synthesis. Should this be true, the consequence would be that uric acid also is found in the organism by synthesis from ammonia and carbonic acid.

I.—AMMONIACUM CAUSTICUM SOLUTUM.

SAL AMMONIAC GAS.

Ammonia—sal ammoniac gas—NH_3 is a colorless, peculiarly and painfully sharp smelling gas, of strong alkaline reaction which, by the aid of great pressure and cold can be condensed into a colorless fluid. It is absorbed in very large quantities by water.

When bubbled through cold water, the gas is quickly absorbed, heat being given of. The water becomes specifically lighter, the more ammonia it contains. 1 liter of water can absorb 600 liters of ammonia. If we imagine the ammonia combined in this solution with one equivalent of H_2O, ammonium hydroxide NH_4OH (which is unknown) being formed, then the similarity with the caustic potash and caustic soda solution would be a very close one. After these two compounds the former is certainly the next strongest base.

The officinal preparation is said to have the specific weight of 0.960 which is equal to about 10 per cent. of ammonia. Because of the strong caustic taste it is called solution of caustic ammonia, or the spirit of hartshorn, it is clear, colorless, of a strong ammoniacal odor, strongly alkaline reaction and combir es with acids to form ammonium salts.

PHYSIOLOGICAL ACTION.

The local effect of ammonia upon the skin and mucous membrane is less intense than that of the caustic alkalies, but probably dependent upon a similar alteration of the tissues as is produced by the latter, such as the withdrawal of water and the decomposition of the albuminoids, swelling and solution of

the surrounding tissues and horny substances.* On account of its volatility and the possibility of inhaling it, the effect of ammonia is spread over a longer portion of the organism, that is to say it can affect the respiratory organs. Apropos of the latter we must mention the fact, that ammonia, like the alkalies, favors the solubility of mucine in mucus and thus renders the mucus more fluid. The following phenomena depend upon these local effects of ammonia.

Skin.—A feeling of warmth, burning and pain. When applied in concentrated solution we have produced inflammation of the skin, exudations and the formation of blisters, and indeed a burning of the deeper layers of the skin, changing them into a smeary paste.

Mucous Membranes of the Digestive Tract.—Smaller doses and greatly diluted solutions, even after long continued use, do not cause any sensible disturbances, except a sharp alkaline taste; it causes a neutralization of the gastric juice, however, just as the alkalies do.

Concentrated solutions or very large quantities cause a severe inflammation of the stomach and intestines with a shedding of the epithelium, production of large quantities of mucus, hemorrhages, severe pains, vomiting and, now and then, diarrhœa. The caustic action upon the mucous membranes may lead to perforation in various places. Should the poisoning not be fatal, a most persistent gastro-intestinal catarrh may remain.

Mucous Membranes of the Respiratory Tract.—Even smelling of a dilute solution produces, in addition to the disagreeable odor which is the result of the impression upon the olfactory nerve, a painful sensation due to irritation of the trigeminus. As a reflex result of this irritation, we have increased secretion of tears (also partly due to direct irritation of the conjunctiva) and severe sneezing. When ammonia gas is inhaled in concentrated form by men or beasts through the nose or mouth, we have an intense irritation of the mucous membranes produced, and as a reflex result severe cough, narrowing of the chink of the glottis and dyspnœa. According to Knoll, if animals are permitted to inhale diluted ammonia gas through a trachea canula, the respiratory movements are stopped during the period of contraction of the diaphragm, owing to a tetanus of the vagi during inspiration. But this is not a specific effect of the ammonia, since similar symp-

* Compare page 33.

whether these be laid in the form of plates (as gold plates) upon the skin and mucous membranes, or whether they be administered internally in the form of a soluble salt, as for example auro-sodium chlorate 0.01:1.5 aq.· dest.—10 drops several times a day. Magnets have an effect similar to that of the active metals.

Passing over many, in part, physiologically interesting facts we shall here limit ourselves to the following. The fact that sensibility is temporarily restored to a part affected by anæsthesia of hysterical origin by the application of metallic plates cannot be questioned, although even this procedure, as well as the application of magnets has often failed us (Nothnagel) even in hysterical cases. As an explanation of these apparently mysterious results, it was supposed that minimum currents of electricity were thus produced; but the fallacy of such an idea is demonstrated by the often observed fact, that plates of bone and wood and the application of mustard plaques is followed by the same effect. A hypothetical explanation lately advanced by Schiff, that the changes in the molecular structure of the nerve produced by hemianæsthesia, are possibly neutralized by the successive molecular shocks which emanate from the metallic plates, seems to fail in explaining the matter any more clearly.

The explanation of this subject by Rumpf is somewhat clearer. He finds that analogous phenomena, namely, the wonderful interchange of sensibility between the two extremities are produced even in healthy people by mustard plaques and metal plates. According to Rumpf then, the action of the metallic plates is to be explained at first by the difference in temperature between the skin and the plate, and later on by the production of a slight irritation, due perhaps to the difference in the conducting power of heat between the metal and the skin. The physiological effects of metallotherapy (according to Westphal) are a local, peripheral, and perhaps a central change in the circulation of the corresponding portion of the central nervous organ. We are of the opinion, however, that a considerable portion of the effect, especially in the best subjects for these investigations, hysterical patients, is due to psychical influences.

ALUMINIUM.

Aluminium, as the active base of clay and loam is one of the *most generally* distributed elements in nature. Its oxygen *compounds have* much weaker basic properties than the alkalies

and alkaline earths, so that they bear the same relation to these as do the weaker acids. Of the many combinations of this metal, potash alum alone is used in therapeutics, and indeed this salt seems to be physiologically the most active of the aluminium compounds, thus rendering the other alums (such as the double sulphates of aluminium and manganese, aluminium and iron and the sulphates of aluminium and the alkali metals, sodium, ammonium, caesium and rubidium) superfluous.

ALUMINIUM AND POTASSIUM SULPHATE—ALUM—POTASH ALUM—ALUMEN.

Alum $(SO_4)_2AlK+12H_2O$ presents large colorless and transparent octahedral crystals, of a sweet puckery taste, dissolving easily, especially in hot water, and having a weak acid reaction. When heated this substance loses its water of crystallization entirely, and is changed to a white, voluminous powder that is slowly soluble in water, and which is known as "burnt alum" or "alum ustum."

PHYSIOLOGICAL ACTION.

Alum coagulates and precipitates dissolved albumen; the burnt variety also withdrawing water to a certain extent, and upon this depends most of its physiological effects.

On the *uninjured* skin it has no evident action and is unable to pass through the epidermis. On the mucous membranes it produces, in very dilute solutions a feeling of dryness in the mouth and a puckery taste. It causes a drying up of the secretion of ulcers of the skin and mucous membranes, by coating them with an albuminate.

In inflamed mucous membranes of any locality and in wounds it causes a contraction of the bloodvessels; this, at least, is the commonly received theory of its action. We did not see in most cases any evident alteration, as far as could be ascertained by direct measurements upon the mesentery of the frog, in the size of the bloodvessels where alum solutions were dropped upon them (Rosenstien, Rossbach); often, however, in the remaining cases an expansion, and only twice a slight contraction was noticed; the capillaries alone were generally expanded; and yet a stasis in the circulation often occurred. Under any circumstances this much is positive, that alum, as far as its contraction upon the vessels is concerned, can not be compared with argentic nitrate or plumbic acetate.

In very concentrated solutions it has a caustic effect upon mucous membranes and sores.

Internally administered, the long continued use of small *diluted quantities* (0.05–0.1) produces a diminished appetite,

disturbances in digestion and constipation. In larger doses it causes inflammation, vomiting and diarrhœa. Given in substance it produces gastro-enteritis and a caustic effect upon the mucous membrane of the stomach. From the gastro-intestinal canal it is probably absorbed as an albuminate and is found in the various organs, and also in the urine (Orfila). It was formerly believed that in the circulation and in the organs a similar effect was produced to that which it exerts locally upon the mucous membrane. But this is not possible for any of the metals, for in the very act of absorption into the blood their affinities are satisfied, while the local effect of alum upon the mucous membranes depends upon the fact that it is there satisfying its affinity. Alum albuminates would not have a puckering or drying effect even locally.

Besides this it prevents decomposition of organic substances, and destroys the foul odor of decomposition.

THERAPEUTIC APPLICATION.

Generally speaking, the indications given for the use of tannic acid and lead acetate hold good for alum. As a matter of fact, however, the latter is much more limited in its application, being never used to produce any internal effect after it has been absorbed into the blood; for this latter purpose it is entirely useless.

The application of alum is mostly in the production of a direct local effect. For this purpose it can be used in all the conditions in which tannin or ferric chloride are used. It should, however, not be given for diarrhœa, because it disturbs digestion; in epistaxis it is superfluous, for when the latter can not be stopped by the use of the tampon, we apply liquor ferri perchloridi. In gonorrhœa tannin is preferred, while in hæmoptysis its effect is imaginary. Its real utility is limited to the following cases: As an injection and for saturating tampons in chronic leucorrhœa; as a gargle in chronic and sometimes sub-acute angina (popularly employed in combination with Salvia tea); and as a wash for perspiring feet.

Magnus has recently recommended the alum pencils in catarrh, blenorrhœa, and medium cases of granular lids; he prefers it to copper and zinc, because it is possible to graduate the strength of the application, and because the duration of the after pain is short. In a similar manner Frankel recommends the alum pencil, finely pointed, in various kinds of uterine leucorrhœa (after gonorrhœal infection; in scrofula and

chlorosis, after abortion and child-birth), because alum is entirely dissolved in the uterus, and has but few dangers and contra-indications. Furthermore alum is used for inhalations. For fuller indications for its use in the latter connection, and for a knowledge of its relations to tannic acid, we would refer to the latter preparation.

Dosage and Preparation.—1. Alumen, 0.1–0.5 per dose (3.0 per day), in powder, pill, or mixture. Externally in the form of powder or solution (1–10 to 150.0–200.0), for inhalation, 1.0–5.0 to 500.0.

2. Alumen ustum (compare with above) applied only externally, has a stronger effect than ordinary alum, and may even produce a slightly caustic effect upon mucous surfaces and wounds.

3. Serum lactis aluminatum—alum whey.—To 100 parts of cow's milk take one of powdered alum. Dose, a glass full. As to its application, compare with article on whey.

APPENDIX TO ALUM.

The following compounds have an effect similar to alum:

1. Aluminium Oxidatum—alumina hydrata.
2. Aluminium sulphuricum.
3. Aluminium aceticum—earnestly recommended by Burow, for application to the surfaces of wounds with putrid secretions, or to ill smelling perspiring surfaces. According to P. Bruns and Maas, the aluminium acetate is an extraordinarily active antiseptic, much stronger than thymol and salycilic acid. It is therefore recommended for wounds that are in a septic condition, as a permanent irrigant used in, at most, a 3% solution. According to Fischer and Muller, solutions of this strongly antiseptic material, as well as dressings that have been saturated in it (aluminium acetate gauze), possess many advantages over carbolic acid solutions and carbolized gauze. For the antiseptic does not evaporate, but always maintains the same strength; nor do irritation or general toxic symptoms follow its use; finally aluminium gauze is soft and easily applied. But the aluminium acetate must not be used for disinfecting the hands or instruments, since it gives the former a rough appearance, while the latter are rendered dull and dirty by it.
4. Argilla (or Bolus alba), the lithate of aluminium, is insoluble in water and acids, and therefore not absorbed into the body, and inactive; it was formerly considered as similar to alum, and used in a like manner. Now it is used only as a constituent of pill masses when such easily decomposed substances as argentic nitrate are to be administered in pill form.

LEAD AND ITS COMBINATIONS.

Lead and many of its combinations are insoluble in water, and must therefore be converted into soluble combinations, before they can become active. But when they are thus converted their general effect, after long continued use, is the same as that of the soluble preparations. The latter are distin-

guished from the former only in the local and acute changes which they produce upon the skin and mucous membranes.

PHYSIOLOGICAL ACTION OF THE LEAD SALTS.

No preparation of lead can be absorbed into the blood by the unbroken skin. Contrary opinions, as for example the statement that lead is absorbed into the body when used as a face powder, need further confirmation. But these salts are easily absorbed through wounds, ulcers of the skin, and through all of the mucous membranes. We must distinguish between a local effect of small and large doses of soluble lead salts, and the general effect of all lead preparations, even if both kind of effects can be ultimately referred back to the same cause, namely, to the relationship existing between lead and albuminoid bodies with which it forms lasting combinations.

LOCAL EFFECTS.

Even concentrated solutions effect no evident change upon the unbroken skin, except that after the fluid, in which the lead salt was dissolved, evaporates, we find the epidermis closely covered with white layers of lead salt.

Lead solutions produce the following changes upon mucous membranes: There is at first a severe, and then a disagreeable, puckery, metallic taste. Upon all mucous membranes, even moderately diluted solutions produce a deposit of lead albuminate, diminution in the various excretions, coagulation of the albuminous components of the superficial cells, with shrinking together of the latter. As a result of these changes we have dryness in the mouth and pharynx, digestive disturbances, diminution of the intestinal secretion and peristalsis, and finally constipation.

Extremely concentrated solutions produce death of the upper layers of the mucous membranes, a white firm coating is formed, which after a time is thrown off, leaving an ulcerating surface underneath the coating. The mucous membrane is at first white and contains little blood, but later on becomes inflamed (Mitscherlich).

The consequences of this corrosive action when the drug is administered internally, are similar to those produced by internal administration of other metallic salts, only less intense. *They are those of* gastro-enteritis; burning, severe pain in the *stoma* [illegible] *itestinal* region, vomiting, diarrhœa, and death.

Should these local affections heal, we may still have symptoms of general lead poisoning, occurring even weeks after.

Upon sores a firm, plaster-like covering of the albuminate of lead is formed, so that formerly moist and suppurating surfaces become dry and heal with extraordinary rapidity under the protection of the layer of lead.

It causes a contraction of the superficial capillaries of mucous membranes and ulcers, but to a less extent than is produced by argentic nitrate. Observations upon the mesentery of a frog show that upon the application of a 50% solution, the arteries and veins are made to contract to about half of their diameter, while the lumen of the capillaries remains unchanged. Very often a stasis in the circulation of the affected portion of the membrane is produced. The surrounding cells become clouded—generally, coagula, composed of white blood corpuscles form in the vessels, which, adhering to the walls, produce a further contraction of the lumen of the vessel. (Rosenstien, Rossbach.)

The principal local effect, then, of diluted lead solutions, is a diminution of the secretions of mucous membranes and ulcerating surfaces, and a narrowing of the bloodvessels.

GENERAL EFFECTS.

Lead is gradually absorbed, when applied locally to ulcers or mucous membranes, or even when inhaled through the bronchial tubes. The most severe symptoms of chronic lead poisoning set in when, as is the case with those who work in lead, only small quantities of lead are introduced into the body at a time, and this is continued for a long time. However, the medicinal administration of lead, even when not continued for a long time, but 3–10 grms. having been introduced, has been followed by symptoms of general poisoning.

Destination of the Lead in the Organism.—In the stomach the lead preparations when taken in moderately diluted quantities are most probably changed in the acid chyle into albuminates, and as such, are absorbed into the circulation, and there transported, as are all metals, by the blood globules (not by the serum, Millon) to the different organs ; so that, after death no more lead is found in the blood, but only in the organs, in the cells of which it exists as an albuminate. As such it remains in the body with great persistency, being only slowly and gradually excreted, partly with the bile and partly with the urine. *Only in albuminous* urine is the quantity of lead increased.

The lead which passes with the bile into the intestines, is partly reabsorbed and partly altered into lead sulphide, as is also the lead albuminate passed into the intestines from the stomach, by contact with the sulphuretted hydrogen of the intestines, and excreted with the fæces which thus assume a black color.

Acute general lead poisoning can not be produced by the ordinary lead salts, for reasons already stated in the general remarks on the metals (page 116). But according to Harnack, such a condition can be produced in all animals by the use of the triethyl lead acetate, $[Pb(C_2H_5)_3C_2H_3O_2]$ With the following prominent symptoms: 1.—Lead affects the substance of all striped muscular fibers (which is especially observed in frogs and rabbits); not that it makes all contraction impossible, but it produces a rapid exhaustion of the activity of the muscle; finally the muscle loses its irritability, dies and falls into a death-like rigidity. 2.—Lead has an irritating effect upon a part of the central motor apparatus, probably the medulla and cerebellum, and thus causes, especially in dogs, cats and pigeons, peculiar ataxic movements, together with continual movements and spasms, and finally convulsions, consciousness and sensation being maintained. 3.—Lead irritates certain nervous apparatus situated in the intestinal wall, which controls the movements of the intestines, and thus produces general contractions and powerful peristaltic movements in the intestines, attacks of colic, increased sensibility of the whole abdominal region and sometimes even purging. No effect is seen upon the unstriped muscular fibers of the intestines and bloodvessels. Respiration and circulation are not directly influenced, although finally both the cardiac and respiratory muscles take part in the general muscular paresis.

It will be seen then, that the acute general effect of the triethyl lead compounds bears a marvelous similarity to the already well known symptoms of chronic lead poisoning.

Symptoms of Chronic Lead Poisoning in Man.—These have been noticed both in cases of poisoning caused by the medicinal administration of small doses, and also in workmen whose occupation has exposed them to the absorption of lead. They resemble the symptoms observed in mercurial poisoning. A disagreeable, constant metallic taste in the mouth, sometimes a grayish discoloration of the edges of the gums; bluish or smoky gray spots upon the mucous membrane of the lips and cheeks, in which little black bodies can be seen with the microscope, partly collected around the vessels and partly lying free

in the tissues (Renaut); also a swelling of these mucous membranes, salivation, impure breath, diminution of the appetite and constipation. A gradually increasing leanness, and a dry, pale, cachectic looking skin.

Frequent attacks of so called lead colic take place; setting in suddenly and characterized by very severe abdominal pain, extending over the whole of the abdomen or limited to single parts, as for instance, around the umbilicus; at the same time, the abdominal wall is generally contracted and of a tense hardness; sometimes greenish, ill-smelling matters are vomited; generally the bowels are constipated for many days, rarely normal or loose. The pulse at this time is generally slow and of a peculiar hardness.

Later on, peculiar neuralgic pains, which are difficult of localization and which appear to have their seat in the joints, bones and muscles of different parts of the body. Sometimes they resemble strong electric shocks, at other times they have a tearing character, increased in intensity in the warmth of the bed at night and also by active motion and diminished by direct pressure; these are called lead arthralgias. Gradually a tremor sets in in single or many muscles; this tremor may increase in intensity until the whole body becomes convulsed. The muscles sometimes resemble hard uneven swellings.

From this condition of the muscles, characteristic lead paralysis is developed, the extensor muscles of the extremities being first affected, while contracture of the non-paralyzed antagonists gives the extremities a peculiar position. The paralysis may affect, later on, the muscles of the trunk and larynx. In the course of time, atrophy of the paralyzed muscles sets in.

Finally, disturbances in the central nervous system set in. (encephalopathies), sometimes in the form of delirium or some disturbance resembling melancholia or mania, and sometimes in the form of general epileptoid convulsions with loss of consciousness.

Reliable observers have not seen disturbances in the liver, spleen or kidneys.

Death set in after the patient had undergone much wasting, owing to the diminished nutrition; dropsies were also sometimes present. Neither the colic nor the muscular paralysis, nor the disturbances in the functions of the brain or spinal cord had a direct influence in producing the fatal result.

At the autopsy of a case of lead poisoning extending over years, *Kussmaul and* Maier found chronic catarrh of the *stomach, intestines* and ductus choledochus, extensive atrophy

of the mucous membranes of the jejunum, ileum and the upper portion of the colon, fatty degeneration of the muscular coat, especially of the small intestine, finally hypertrophy and sclerosis of the connective tissue of many of the sympathetic ganglia; especially of the coeliac and superior cervical ganglia, with diminution of the ganglion cells.

In Animals.—Since the observations on men leave much to be desired as regards completeness, we consider it well to add here the accurate observations of Heubel on dogs, which he poisoned in four weeks, by gradually increasing doses of from 0.2 to 0.5 grms. of lead acetate.

But few of the dogs retained their normal appetite to the time of death. Most of them soon lost their appetite and began to vomit, their thirst increased and sometimes they suffered from diarrhœa; frequently from salivation. These symptoms diminished in intensity or entirely disappeared for a short time only to return again.

Both the animals that maintained their appetite until death as well as those that suffered from severe digestive disturbances, showed great wasting of the whole body, and particularly of the back muscles and the hind leg. The weight of the former was diminished by 20–40 % of the original weight, while the latter showed a diminition of 50 %. The wasting can not, therefore, be entirely due to the digestive disturbances.

Attacks of colic were rare; they generally occurred suddenly, while the animal was seemingly well. They were evinced by violent cries of pain, and disappeared after half an hour as suddenly as they had come. The dog then again lay quietly as before the attack; ate with appetite and drank a great deal. Relapses often occurred.

Actual lead palsy has not yet been observed in animals: the muscles, it is true, waste away and evident weakness of the hind legs occurs, often even tremor, but never complete muscular paralysis; perhaps on account of too short a period of probation.

In the 4th or 5th week the appearance of the so-called epilepsia (s. eclampsia) saturnina occurs. Again without warning, except that diuresis is often diminished for a long time previous. The animals fall suddenly, generally with a loud cry, to the earth and are seized with violent convulsions, sometimes lasting an hour. The excretion of saliva and mucus is considerably increased; the pupils are dilated and inactive. Urine and fæces are passed involuntarily. When not convulsed the animal is in a sleepy or comatose condition.

During the first three weeks of the poisoning the urine is plentiful and presents nothing abnormal. Later on the quantity of the urine rises and falls and the biliary coloring matters begin to appear in it. Albumen is never and blood seldom found in it.

Fæcal evacuations, even at the very beginning, became fewer and toward the end almost entirely stopped. The fæces were darker—almost black—of firm consistency, but not dry. Only when severe digestive disturbances set in were these evacuations more frequent and fluid.

At the autopsy a general disappearance of the fat in the body was found. The greatly reduced muscles had a normal appearance. Brain and spinal cord were of a softer and more fluid consistency. Lungs, heart and bloodvessels were normal. The heart muscle was not atrophied. The liver was generally well supplied with blood; the gall bladder always swelled and filled with a dark green bile. Spleen, kidneys and pancreas were smaller and contained less blood than normal. The gastro-intestinal mucous membrane showed no change with the exception of a light gray discoloration.

EXPLANATION OF CHRONIC LEAD ACTION.

There are still some difficulties in the way of this explanation, although since the last appearance of this book several superior writers have busied themselves with its solution. We can not, therefore, give a connected story, but must be satisfied to enumerate the individual facts concerning its action which have been contributed by Heubel, Harnack, Riegel and Remak. Heubel bases his theory entirely upon the varying proportion of lead and water contained in the different organs. In this way he certainly proves the fallacy of former views, but does not prove his own.

Harnack draws his conclusions from observations upon animals poisoned by the lead triethyl (page 124) and observing the similarity between acute, general and chronic poisoning, believes that both sets of symptoms are due to the same organic changes. Riegel bases his conclusion upon observations of the pulse alone and Remak traces all the symptoms back to the lead palsies.

Heubel attempts most of all to disprove the theories of Henle, Hitzig and Gusserow. According to Henle, lead exerts an astringent effect upon the circulatory apparatus just as it does *locally, and thus* produces a contraction of the involun-

tary muscular coat of the vessels. "By the contraction of the arteries the blood is collected in the veins, the latter on account of their dilatation press upon the nerve trunks, which results at first in arthralgia and convulsions and finally in anæsthesia and paralysis. The same affection of the involuntary muscles of the intestines and bladder produces colic, while the venous hyperæmia of the cranial contents leads to encephalopathic symptoms." While Henle believes that a general narrowing of the caliber of the arteries produces a diminution in the quantity of the various fluid excretions, and therefore an increase in the plasma of the blood, Hitzig, reasoning from the same premises, deduces an entirely different set of conclusions: An abnormally filled arterial system and stasis in the capillaries, leads to an increase of the excretions, and diminution and greater concentration of the mass of the blood. Gusserow concluded, from the fact that he found a large percentage of lead in the muscles, that a direct change was produced in these by the lead. Traube thought the cerebral symptoms uræmic and due to a lead affection of the kidneys.

Heubel reasoned from the proper assumption that those organs or tissues upon which a drug exerts a specific action, probably have a peculiar affinity for this drug and therefore absorb into their substance a relatively larger percentage of it from the circulation than other tissues. "In the beginning the blood must contain the largest percentage, not because it has the greatest affinity for the substance, but because it is the absorbing fluid which finally yields up the poison to the tissues. The excretory organs contain larger quantities because the poison passes through these before it is entirely excreted." He found that in dogs chronically poisoned with lead (page 117) accurate quantitative observations always showed that the percentage of lead always remained relatively the same, as is shown by the following table, which represents the tissues in diminishing series:

Bones Kidneys Liver	With a relatively large percentage of lead.
Brain Spinal Cord	With a much smaller percentage of lead.
Striped voluntary muscles Unstriped intestinal *muscular* coat	With a still smaller percentage of lead.
Blood—	Only traces of lead.

Since the striped as well as the unstriped muscles contain less lead than almost all of the other tissues, then, according to Heubel, the theories of Henle and Gusserow which seek to explain the lead effects by the changes which it produces in the muscles, fall to the ground. And since the central organs of the nervous system contain a relatively larger amount of lead than most of the other organs, with the exception of those concerned in excretion, the conclusion seems warranted that the nervous tissues have the greatest chemical affinity for lead and since this tissue reacts much more strongly to small quantities of the drug than other tissues do to large ones, he, following Tanquerel des Planches, explains almost all of the poisonous symptoms by changes produced in the nerve tissues.

According to Heubel the lead colic does not depend upon spasm of the muscular coat of the intestines: "for such a spasm would hasten rather than hinder the passage of the fæces through the intestines, apart from the fact that a spasm could not last for weeks as does this colic. It must therefore be accounted for by a diminution in the peristaltic movements of the intestines due to a paralytic condition of the intestinal ganglia or to an irritation of the splanchnic nerves. In this way, also, the constipation which manifests itself in the later stages of the poisoning can be explained. The pains accompanying the colic are not the result of spasm, but purely neurotic." Harnack explains the lead colic as due to irritation of the intestinal ganglia by the lead, resulting in disturbances in the functions of the intestines, as for instance the obstinate constipation in man which follows as a result of the long continued spasmodic contraction of the intestines, or the diarrhœa, occurring in animals, due to the increased peristalsis; the intense pain, he thinks, depends upon the severe intestinal contractions, the peritoneal covering acting in sympathy with the intestine and thus producing pain. The contracted condition of the abdomen, together with the extreme hardness of the abdominal wall, he explains by a reflex contraction of the abdominal muscles.

The theory of a general spasm of the muscular coat of the arteries is, according to H., not well founded and "is in no way proved by the fact that the pulse is hard; the radial pulse is indeed hard, but not small; the artery is not contracted, but well filled and tense, the pulse being large. The frequency of the pulse is diminished, although a narrowing of all the arteries and increase of the blood pressure ought to increase it. We should suppose then that the peculiar character of the pulse

is due rather to an abnormal distribution of the blood, than to an arterial spasm.

In favor of this view is also the fact that this peculiar pulse only occurs during the attacks of colic. The slowing of the pulsation of the heart is a reflex effect of a centripetal irritation transmitted by the splanchnic nerves. Hitzig's view, that the lead circulating in the arteries has the same astringent effect upon them, as it has on external application upon mucous membranes and ulcers is not tenable for the reason that only traces of lead are found in the blood and there in the form of albuminates. No metallic abuminate has the local effect of the free metal." Riegel believes that an attack of lead colic is accompanied by an enormous irritation of the vaso-motor nerves which causes an increased tension of the arteries and as a result, intestinal pain ; during such an attack the pulse becomes slower and large and has the same character as when the aortic pressure is increased. With a dimunition of the pain the character of the pulse is also changed ; increased tension of the vessels, diminution of the quantity of urea and severity of the colicky pains are associated conditions. According to Harnack, the general contraction of the intestines drives a considerable quantity of blood out of the intestines into other parts of the vascular system, which produces a filling up and increased tension of the arteries and a slowing of the pulse. The excretion of the saliva and bile is rather increased than diminished ; the temporary diminution in the urine excreted during an attack of colic is also due to irritation of the branches of the n. splanchnicus major in consequence of which the blood supply to the kidneys is diminished.

The lead palsy is according to Heubel dependent upon paralysis of the motor nerves and not of the muscular fiber itself. Only in consequence of general nutritive disturbances do the muscles in lead palsy atrophy more rapidly than in other forms of paralysis. The rapid loss of faradic as well as of galvanic contractility does not by any means point to a primary disease of the muscles; not until years after the beginning of the lead palsy, is there seen, according to Duchenne, any noticeable change in the texture or any fatty degeneration of the muscular fibers. The fact that of the muscles supplied by any particular nerve trunk, as for instance the radial nerve, all are never paralyzed, but only certain ones, seems to indicate that the affection is one of the peripheral nerves. Remak affirms, however, that in lead palsy those muscles are generally affected which are functionally associated and which have a

similar action although they are innervated by different nerves. He therefore believes himself warranted in the conclusion that lead palsy is of central origin and due to an affection of adjacent groups of ganglia lying in the spinal cord. Harnack, however, thinks the lead palsy due to an affection of the substance of the striped muscular fibers. The fact that the muscle is not, at first, rendered inexcitable but only so as to be rapidly tired out explains why a muscle affected by lead palsy, is not thrown into contraction by induced currents, while it does react to the galvanic current. Renaut observed in two patients affected by lead poisoning a febrile condition preceding the appearance of paralytic symptoms, just as is the case in spinal paralysis of children or adults. He considers this a new confirmation of the theory which supposes lead palsy to be the result of a sub-acute poliomyelitis. The chronic cerebral symptoms are also to be considered as direct results of the lead action; but it is possible that the epilepsia saturnina is of uræmic origin, as Traube supposes.

Relapses occur in lead poisoning. The large percentage of lead contained in the bones explains why it is that patients who have apparently been well for years and who have carefully avoided every means by which lead might regain an entrance to the system, at times again present new symptoms of lead poisoning. The tissue metamorphosis in the bones being slow the lead remains in them for a long time after it has been excreted from the other organs, and is thus again, later on, carried to portions of the body that have an affinity for it. Besides this Hermann has shown that the relative percentage of lead in the bones is much lower, when the amount of lead is determined, not by that contained in the fresh organs but from the solid constituents as a basis.

Tissue Metamorphosis.—Metamorphosis going on in the body undergoes many changes under the influence of lead. There is considerable anæmia. There is an increase of uric acid in the blood in consequence of the occurrence of gouty attacks, and finally there is a change in the amount of water contained in the different organs. Heubel has found the percentage of water in all of the organs (brain, spinal cord, lungs, salivary glands, liver, spleen, kidney and muscle) increased by 0.6–3.0 per cent. The blood itself showed a diminution in the solid constituents, in chronic lead poisoning, (24–50 per mille) and a proportionate increase in the amount of water, a *diminution of the blood* corpuscles (20–40 per mille) and of

the percentage of albumen (4, 5, 7.5 per mille), and finally a slight increase in the extractives and salts.

I.—NEUTRAL LEAD ACETATE—PLUMBUM ACETICUM.

The neutral lead acetate, lead diacetate $(CH_3CO.O)_2Pb.+3H_2O$—also known as sugar of lead and saccharum saturni, is made by the solution of litharge in vinegar. From this solution it crystallizes in four-sided prisms. These crystals effloresce in the air, and dissolve in 1½ parts of water and 8 parts of alcohol.

THERAPEUTIC APPLICATION.

Plumbic acetate is a decidedly active agent, but its actual therapeutic value is less than is generally supposed.

In the first place it is used as a hæmostatic in hæmorrhages from internal organs and most of all in hæmorrhages from the lungs, under the following conditions:

If the hæmorrhage be due to an aneurism or comes from a large cavity into which an arterial branch opens, lead or any other styptic is certainly useless. On the other hand we know that very slight hæmoptysis, in which only a few bloody sputa are expectorated, ceases under proper dietetic precautions without drugs; so that here lead is superfluous. But in frequent hæmoptysis of severe or medium intensity, or where the attack is persistent lead acetate will generally stop the hæmorrhage. The less of febrile movement there be present the better fitted is sugar of lead to the case. If there be a tendency to cough it is best to combine the styptic with morphia. The expected result, however, generally occurs only when large doses are administered; namely 0.05 every 2 hours; in profuse hæmorrhage it may at the outset be administered every half hour or hour. Experience teaches that poisoning need not be feared. Digestive disturbances are contra-indications for the use of this remedy, but if the hæmorrhage is severe and danger be present we may even in these cases be driven to the use of lead. We must, however, acknowledge, that an extended experience has taught us, that even these somewhat serious hæmorrhages sometimes cease under the influence of morphia, (to allay the cough), and the proper dietetic conditions, without the use of any styptic; *so that the action of the lead acetate even in these cases becomes a matter of doubt.* Lead acetate is also used for hæmorrhages from the stomach and intestine; it is better here, however, to make use of other remedies, which are generally of greater utility, since the bleeding point is here accessible, and furthermore since these disturb the digestion less (ice internally and externally, also tannin and liquor ferri sesquichlorati). In

uterine hæmorrhages lead is superfluous. Should these occur during labor, we have the secale preparations and other proceedures, while in the non-pregnant condition local applications are of greater utility.

In diarrhoea lead acetate is much used, and with much success. But since in most of the cases other remedies and appliances, which do not disturb the digestive functions, are perfectly successful, experience has taught us to use the acetate of lead only in those chronic cases in which the diarrhœa is due to a chronic ulcerative process of the mucous membrane of the intestines. It is for this reason that opium combined with lead acetate is the only remedy which, as superior observers have shown, in any degree controls the diarrhœa depending upon tuberculosis of the intestine.

The lead acetate is also used as an astringent in bronchoblenorrhœa, with or without brochiectasis. Sometimes it is possible to control the superfluous secretion by the long continued use of lead, and these are the cases of so-called consumption (phthisis pituitosa), which the older writers report as cured by lead. Recent experience has also taught, however, that these very cases are improved by proper inhalations, and for this reason the use of lead, which if long continued is apt to produce undesirable symptoms, is limited to those few cases in which inhalations are impossible for external reasons, or in which there is present at the same time a tendency to hæmorrhages from the bronchial mucous membrane. Against hyperidrosis, as occurring in the course of consumptive and febrile diseases, especially in phthisis, the lead acetate is sometimes of great utility. Laennec, indeed, believed this "almost the only remedy" against the sweating of phthisis. But now we have a better remedy in atropine; for in addition to the fact that we are sometimes disappointed in the use of lead, its long continued use may be followed by disadvantageous results. We should also observe that in acute œdema of the lungs we have seen decided benefit result from the use of lead acetate in large doses (0.05 half hourly), and at the same time the application of large blisters (used at first, we believe, by Traube). We here speak of that form of œdema of the lungs which occurs in the course of chronic nephritis, with general dropsy. Furthermore, in the pneumonia of topers, or in those individuals in whom there is a tendency to profuse sweating, at the height of the fever lead acetate is said to be useful. But whether the *principal part of the* result is not due to large vesicants is *doubtful: again*, the favorable effect is not uniform.

Formerly lead acetate was used in various acute inflammatory affections as an antiphlogistic, but experience has not shown that this application is of any utility.

In a few conditions of this kind the remedy is still used, but only to fulfill certain indications, and not as an antiphlogistic.

The use of this Drug in *Pneumonia*.—In the ordinary course of this malady plumbic acetate is entirely superfluous. It is only when the dangerous complication of œdema of the lungs sets in that it is indicated. A second indication for its use, also, is when the pneumonia is of the character known as "hæmorrhagic," and here it it is indicated as a hæmostatic.

Another acute inflammatory affection in which lead is preferred is acute hæmorrhagic nephritis, although we have seen no good results follow its use. It is used after the ordinary antiphlogistic treatment and hydragogue cathartics have been administered. In *acute articular rheumatism* (Munk) we can do very well without this preparation. Traube recommended it for gangrene of the lungs; that is to say in that form in which only one or two gangrenous cavities are present. But our experience in its use for this affection is limited, as at present the inhalation method is the most commonly adopted.

It goes without saying that the use of the lead in any of these diseases must be carried on with much care, the drug being suspended at the first signs of any of the above given toxic symptoms. In addition to the contra-indication already mentioned, namely digestive disturbances, there is another which should be considered when the drug is to be used for a long time—that is arterial sclerosis (atheroma.—Tr.) The further contra-indication, the presence of constipation, is of no importance in the uses just enumerated. The dangers of poisoning are, however, much diminished when the drug is administered with small doses of opium.

Externally, lead acetate is used in the same conditions which we shall enumerate under the head of zinc sulphate, except that in catarrhal conjunctivitis the former is much inferior to the latter for several reasons, such as more rapid decomposition, etc.

Dosage and Preparation.—Plumbum aceticum internally from 0.01—0.05 per dose (ad. 0.05 per dose, ad 0.4 per day in powder, pill or solution.) Externally powdered in substance, or used in 1–10 per cent. solution, or as an ointment (1:10).

2.—BASIC ACETATE OF LEAD—PLUMBUM HYDRICO—ACETICUM SOLUTUM.

This preparation, known also as liquor plumbi subacetici—acetum plumbi vinegar of lead, is formed by boiling the solution (1 part of lead diacetate

and 0.6 parts of lead oxide. It presents a clear, colorless, slightly alkaline reacting fluid, but one which easily absorbs carbonic acid from the air, and thus becomes cloudy, an insoluble lead carbonate being formed.

Physiological Action.—Its local and general effect is like that of the sugar of lead, but it seems more closely allied to the albuminates.

Therapeutic Application.—Lead subacetate is used exclusively for external application, and is a very popular remedy. It is used in excessively suppurating surfaces of the mucous membrane and skin, and in all inflammatory affections of the skin and immediately underlying structures. The commonly received opinion of the antiphlogistic action of lead subacetate is entirely unfounded, although the preparation is used daily with this theory of its action. It does not even pass through the unbroken epidermis, and it is now generally acknowledged that the greatest part of the effect is due to the water or other material with which the lead subacetate is combined in the different forms of application; also to the lower or higher temperature of the application, or to the wax covering which is sometimes applied over the lukewarm lead subacetate compress. The fact that most of the cases in which this application of lead subacetate is successful do just as well under pure water applications, proves the correctness of this view.

Among the conditions in which this drug is used for its antiphlogistic action, we may mention contusions, simple or with extravasation of blood, acute œdematous swellings of the skin, following after any traumatism, frost bites, burns of the first and second degree, eczema, erysipelas, etc.

Dosage and Preparation. 1. Acetum Plumbi. Lead subacetate is only rarely used in its officinal strength; as for example, in condylomata as an astringent. It is mostly used in diluted solutions as an eye wash (which, as we have already mentioned under lead acetate, is of little use). It is used in 1–2 % solution. Ointments are of the strength of 1 part to 5–10 of simple ointment.

2. Aqua plumbi (aqua saturnini), lead water (cooling water); 1 part of lead acetate to 49 of distilled water, as a lotion either in full strength or diluted.

3. Aqua Plumbi Goulardi s. Aqua plumbi spirituosa: lead water (which contains aqua font. instead of aqua dest.), with the addition of 4 parts of spirit. vini rectificatus, as a lotion to the unbroken skin.

4. Unguentum Plumbi—Ceratum saturni. Unguentum nutritum, lead ointment, 3 parts of lead subacetate, 8 of wax, and 29 of lard—drying salve.

3.—LEAD CARBONATE—PLUMBUM CARBONICUM.

The lead carbonate, $PbCO_3$ or white lead (cerussa), is a heavy powder, insoluble in water, and used only for making salves and plasters for inflammations and sores of the skin.

Preparations—Unguentum Plumbi hydrico-carbonici. Unguentum cerussæ s. album simplex, white lead salve; 2 parts of fat, 1 part of white lead; used as a healing (drying) salve.

2. Unguentum cerussæ camphoratum, 100 parts of ung. cerussæ and 5 parts of camphor.

3. Emplastrum cerussæ.—Emplastrum album coctum.—White lead plaster, 10 parts of lead oxide, 18 parts of white lead, 25 parts of olive oil; when fresh is of a white color, which in time turns yellow; not very sticky.

4. LEAD OXIDE—PLUMBUM OXIDATUM.

The lead oxide (litharge) is in the form of reddish yellow powder, or shining scaly crystals, which crumble in the air, being easily converted into a white powder of the carbonate of lead, insoluble in water, but very soluble in acids.

Action.—Lead oxide is used in the preparation of plasters, since when mixed with fat, a lead salt, a combination of the lead with a fatty acid, is the result. Simple lead plaster forms a protecting imperspirable covering to the skin, its healing effect being partly due to the protection it affords from the outer air, and partly to the warmth and moisture resulting from its application. The addition of resins according to their kind, either increases the adhesive power of the plaster or gives the plaster the property of producing an irritant effect upon the skin.

Preparations.—1. Emplastrum plumbi simplex, emplastrum lithargyri s. diachylon simplex, simple lead plaster. Equal parts of olive oil, adeps suillus and litharge, 5 parts of lead oxide and 9 of olive oil, white, only slightly tenacious, not fatty, easily spread, inactive plaster, well adapted for bandaging and compresses.

2. Emplastrum plumbi s. lithargyri s. diachylon compositum. Compound lead plaster or rubber plaster, 24 parts of emplastrum plumbi simplex, 3 parts of yellow wax and 2 parts each of ammoniac gum, galbanum, and turpentine. Yellowish brown, and has, on account of the resins, an irritant effect.

3. Emplastrum adhesivum, sticking plaster, 18 parts of crude oleic acid, 10 of litharge, 30 of colophonium, 1 of sevum, 4 of emplast. plumbi simplex and 1 part of resina pini Burgundicæ, yellowish, of strong adhesive power, but irritant to the skin.

4. Emplastrum saponatum, soap plaster, 72 parts of lead plaster, 6 of sapo Hispanicus pulveratus, 12 of yellow wax, 1 of camphor; is of a whitish color, only slightly adhesive, used in the same way as simple lead plaster.

5. Emplastrum lithargyri molle s. matris album, "white mother plaster" (mutter pflaster), 5 parts of emp. lith. spl., 2 parts of adeps suillus and 1 part each of sevum and cera flava.

6. Unguentum diachylon Hebræ. Hebra's lead salve, emp. litharg. spl. and ol. lini in equal parts.

APPENDIX TO LEAD.

The following preparations are entirely superfluous: hyproxide of lead (Mennig; Minium) a scarlet-red powder insoluble in water.

Preparations.—Emplastrum minii rubrum, of each 100 parts of cera flava, sevum, minium, and ol. olivarum and 3 parts of camphor.

Emplastrum fuscum, s. matris fuscum, black mother plaster, 32 parts of minium, 64 parts of olive oil, and 16 parts of cera flava.

Emplastrum fuscum camphoratum s. nigrum s. universale s. noricum s. Minii adustum black mother and Nurnberger universal plaster, 100 parts of matris fuscum and 1 part of camphor.

Plumbum tannicum pultiforme.—A poultice for bed sores, thrown down by the addition of lead subacetate to an infusion of oak bark.

Preparation.—Unguentum plumbi tannici—ung. ad decubitum—ung. glycerini with tannate of lead for application to bed sores.

Treatment of lead poisoning.—In cases of acute lead poisoning, we should *administer mucilaginous drinks, albumen and milk until the proper antidote can be obtained.* If the lead itself does not cause vomiting we must seek to

produce it by mechanical irritation of the pharynx or by the subcutaneous injection of apomorphine, or the stomach pump or the Heber apparatus may be applied. The best antidotes are the sulphates of the alkalies, as the potassium, sodium and magnesium sulphates: they act by producing the insoluble lead sulphate. In addition to this, however, we must see that the sulphate of lead is carried out of the system by cathartics, such as castor oil or an enema, if the cathartics administered as antidotes have not already caused purging.

In chronic lead poisoning the principal indications are to get rid of the lead from the system, and to treat any of the serious complications or symptoms. There are no antidotes upon which we can depend; the utility of the sulphuric acid lemonade is entirely illusionary. Potassium iodide internally and the use of sulphur baths are of doubtful utility. The most important agents are the prevention of further supply of lead to the system, and the use of warm baths to facilitate the interchange of materials in the body.

Lead colic has been variously treated at different times, generally in accordance with the theory of its causation prevailing at the time. To mention all of these methods would be superfluous. Experience has shown the following procedures to be the most useful. Long continued warm baths, warm poultices to the abdomen, opiates internally or subcutaneously. In obstinate constipation enemata containing castor oil, or cathartics internally (ol. ricini—senna—Epsom salts or Croton oil); where vomiting is also a symptom, ice internally and carbonic acid (effervescing) drinks. The recent recommendation of amyl nitrite, pilocarpine and atropine need further practical confirmation. The arthralgia, anæsthesia and tremor are treated like the general lead cachexia, with warm baths, and perhaps potassium iodide, and if necessary, in arthralgia, morphia may be used symptomatically. In paralyses the methodical application of the galvanic and faradic currents is indicated. The encephalopathies have hitherto remained unaffected in spite of all therapeutic agents.

SILVER—ARGENTUM.

This metal is in many respects allied to lead. It is used very frequently therapeutically but only under the form of the nitrate.

NITRATE OF SILVER—ARGENTUM NITRICUM.

Silver nitrate NO_3Ag (Hoellenstein–Lapis infernalis) is formed by dissolving silver in nitric acid and allowing it to cool, when it is deposited in white crystals, as—

A. n. crystallisatum, these, when melted and cast in form of sticks give us A. n. fusum.

Both of these preparations are easily soluble in ½ part of water at ordinary temperatures, and in such a solution have a neutral reaction.

In a pure condition they undergo no change, but in solution they are changed when exposed to light, or when brought in contact with organic substances; in both cases they undergo reduction and become black; they should, therefore, be protected from the light by being kept in dark bottles.

Nitrate *of silver stains* upon linen are easily removed when rubbed with *potassium cyanide or pieces* of iodine, and then washed with ammonia.

PHYSIOLOGICAL ACTION.

In consequence of the weak combination existing between silver and its acid, silver nitrate, and indeed every silver salt, is easily reduced to metallic silver when brought in contact with other (numerous) bodies and reagents.

Like all metallic salts, the silver nitrate has an intimate relationship to the albuminoid bodies, producing a white precipitate, which soon turns black, from albuminoid solutions. Its affinity for the horny tissues, as, for instance, the epidermis, is even greater than that of the other metals. When albumen and sodium chloride are present at the same time, the silver does not combine with the chlorine until all of the albumen is saturated.

Local effect.—In extensively diluted solution lunar caustic has an astringent effect upon the vessels of the skin from which the epidermis has been removed; it has a similar effect also upon ulcers of the skin, and upon the vessels of all the mucous membranes and ulcers of mucous membranes. Experiments made upon the mesentery of the frog, show that this astringent effect is greater even than that of the lead acetate, affecting at the same time the arteries, veins and capillaries, and causing a slowing, and even a stasis of the circulation in the affected region. The narrowing of the vessels follows rapidly (15–50 seconds) after the application of the solution, without the occurrence of any dilatation either before or after the application.

It is not a reflex result dependent upon a reflex irritation of the vaso-motor center, but it is the result of a local action upon the vaso-motor nerves.

The maximum contraction of the vessel is to about one-half of its original diameter. (Rosenstirn and Rossbach). This action, which can be observed in men and animals, was particularly marked upon inflamed mucous membranes; so that diluted nitrate of silver solutions are among the best anti-phlogistic remedies.

The epidermis is rapidly blackened by the application of silver nitrate, after 3–8 days the blackened epidermis gives place to a newly formed epidermis. If the action, however, be a very intense one, (very concentrated solution), the result is a painful caustic effect upon the skin, an eschar being formed. Inflamed and swollen portions of the skin become pale and diminish in volume. Upon the mucous membranes, dilute solutions produce whitish coagula owing to coagulation of the albuminoid bodies;

the mucous membrane reddened by inflammation becomes paler, the disagreeable symptoms, such as the dryness and pain being diminished. Concentrated solutions of silver nitrate in substance produce a caustic effect upon the mucous membrane, with a burning pain. The ulcer which is left has a tendency to heal rapidly.

The secretion of ulcers or sores is immediately coagulated by silver nitrate. It forms, in the same manner as lead solution, a white protective covering over the sore. The healing effect following the application is partly due to the application and partly to the irritation produced by, especially the stronger solutions, upon the neighboring regions.

The caustic effect of the silver nitrate is always sharply defined and limited to the point of application. The effect does not spread in surface or in depth, beyond the extent of the original application.

Blood coagulates very rapidly under its influence, so that capillary hæmorrhage can be rapidly controlled by its local application.

From what has been said, we can easily deduce the local effects of nitrate of silver when given internally. In the mouth it causes a disagreeable, puckery, metallic taste; and even here it forms albuminates with the saliva and mucus, and chloride of silver with the chlorides of the secretions. In the stomach contents the silver nitrate comes in relation with so many albuminates and so much sodium chloride, that its combining power is satisfied, the result being that it is only when introduced upon the empty stomach, that it attacks the mucous membrane itself. It is for this reason that doses sufficiently large and concentrated to affect the skin, produce no noteworthy effect upon the stomach. It is only in doses of 0.05 grm. upwards that we sometimes notice a feeling of warmth, or even burning pain in the stomach. Diminished appetite only follows after long continued use. Large quantities, indeed, may have a caustic effect upon the stomach, producing also gastritis with severe pain and vomiting—and sometimes even death results.

The silver nitrate as ordinarily used never reaches the intestine as such, but as an albuminate or a silver chloride. The latter is probably produced by the metallic chlorides present in the intestine, and is probably there present in a soluble and absorbable condition.

The portion not absorbed into the blood appears in the *fæces as silver sulphide*. During the use of silver nitrate, the *fæces are of a slimy fluid* consistency.

General Action of the Silver Nitrate.—It is positively known that silver can get into the circulation by absorption from the stomach and intestinal canal. But in what way this is accomplished is a matter of dispute. The generally accepted opinion that it is absorbed into the circulation either as an albuminate or in some other soluble form is rejected by Riemer, on account of one of the findings in chronic poisoning to which we shall refer later on. "It does not diffuse through the intestinal wall as a soluble salt, to be reduced to the metallic form in the blood, and deposited as pigment, but it is reduced in the intestine, and passes through the intestinal epithelium as an element."

In the ordinary form in which nitrate of silver is given, namely, in pills, it is decomposed a few hours after the pills have been prepared. Furthermore, the analogy existing between the course taken by silver through the alimentary canal and the method of the absorption of fat in the middle portion of the small intestine, speaks in favor of its absorption under its own form. The particles of silver were seen most thickly collected at the place where most of the intestinal secretion must be delivered, and where the ducts are so narrow as not to admit the passage of firm inorganic bodies.

Besides this, in chronic poisoning from silver nitrate we never see the same appearances, as when weak solutions of silver nitrate are injected directly into the blood, lymph or interstitial connective tissue; for in these cases the connecting or cementing material of the endothelium combines with the silver solution, reduces it, and thus surrounds the cells by a dark border. When introduced through the stomach a similar appearance is nowhere found. This question, however, could only be settled by feeding animals with reduced silver exclusively. Jacobi's experiments led to partly different results: 1. Rabbits fed on reduced metallic silver, receiving altogether from 5 to 12 grms. in 4 months, showed no traces of the presence of silver in the tissues, either microscopically or chemically, nor was there any found in the liver or kidneys. 2. On the other hand after the subcutaneous as well as internal administration of a soluble double salt of silver (as the hyposulphite of silver and soda), silver was found in the body, although not in the urine. The stomach and intestinal epithelium remained entirely free from the discoloration, but underneath the epithelium was found a dense deposit of black particles of silver. We must, therefore, believe *that the silver which* was administered, probably passed through *the epithelial layer* of the digestive canal, in a soluble form, to be

decomposed and reduced on the other side. Jacobi furthermore shows the great improbability of solid inorganic substances being able to pass through the unbroken gastric mucous membrane, and he believes, furthermore, that the opinions of Riemer are not, in every respect, well founded. "But Riemer is right when he explains the distribution of silver in the body of argyrotics on the theory that reduced silver (but reduced after absorption), is collected together in insoluble particles; in fact, it is accomplished by a sort of metastasis (Virchow)."

In favor of this explanation is (according to Jacobi) the fact that hitherto no other than a local effect has been positively observed to follow the use of the nitrate of silver.

Furthermore, the assertion of Riemer that in the nitrate of silver pills all of the nitrate of silver is reduced in a very short time, is only partly true. The nitrate, it is true, very soon disappears, but it is only partly reduced, and partly changed to the silver chloride.

On the other hand Bogoslowsky's experiments seem to be in favor of the theory that the silver salts are introduced into the blood and tissues in a soluble form, in connection with the albuminates, and that they even produce serious changes in the organs by chemical action; concerning this point, however, more numerous observations are desirable; Jacobi denies the correctness of these conclusions and does not consider it as proven that the silver preparations ever exert any general effect by absorption from the intestinal canal.

In order to exclude the local action upon the mucous membranes, Bogoslowsky made use only of such silver preparations whose affinity had already been satisfied before they were introduced into the organism; that is to say he used the silver peptones and the double salt of silver and soda, which had already been used by Ball, both of these salts causing no coagulation in albumen, and being rapidly absorbed without causing any alteration in the mucous membrane.

The most intense general effect was produced by the double salt. Rabbits died after taking from 2.0–3.0 grms, in 40 days, in single doses of 0.01–0.1 grms. The silver peptone produced death after single doses of 0.05–0.5 grms., had been administered for 43 days, about 4.0 grms. having been given altogether. During these experiments the following functional and organic disturbances occurred: Diminution in the weight of the body, disappearance of the adipose tissue and a chlorotic condition of the blood; a process of degeneration taking place in the muscles and also in the heart, and as a

result of the latter, retardation of the blood throughout the entire venous system; fatty degeneration of the liver, hypertrophy of the kidneys, and albuminuria; catarrhal inflammation of the air passages, and digestive canal, affections of the spinal cord, with symptoms of motor and sensory paresis. Rozsahegyi observed similar effects, together with hyperæmia and hepatization of the lungs in rabbits, into the stomach and under the skin of which he had injected weak solutions of nitrate of silver. Rouget concluded from his observations, made by injecting subcutaneously either the silver nitrate or the double salt, that the motor and respiratory centers are especially affected, upon which he thinks all the other symptoms are dependent.

In man, even after the administration of large doses of the silver nitrate, none of the above mentioned symptoms or organic changes have been observed; nor has the drug been seen to have any influence in shortening life. It is possible that this absence of symptoms is due to the fact that the larger part of the silver is immediately reduced to insoluble metallic silver, in which condition it can at most exert only a physical effect. These particles of silver produce a pigmentation in many organs, which is generally known under the name of argyria or chronic silver poisoning, and which during life is only shown by a grayish black discoloration of the skin of the face. This discoloration and pigmentation can not be removed by the application of any remedy, and generally appears after 30.0 grms. of silver have been taken, it being a matter of indifference whether the remedy has been given for one, two or more years. According to the observations of Frommann and Riemer made upon the dead bodies of people who had suffered from argyria during life, it appears that the granules of silver pigments are found not only in the skin of the face but in almost all of the internal organs, a proof that the reduction is not dependent upon the sun light. It (silver) is never found in combination with the cellular elements, or imbedded in the intercellular substance, but it is rather found deposited in the basement substance of the connective tissue, and in the homogeneous membranes allied to connective tissue. The tissues in which argyria shows itself by preference are the skin, glomeruli of the kidneys, the choroid plexus, the intima of the aorta and the lymphatic glands of the mesentery. It is a remarkable fact that all of the capillary bloodvessels are free from pigment, which evidently speaks in favor of the physical explanation of Riemer. Frommann—Versmann have determined the percentage of silver present in some of the organs

most affected in argyria and find in the liver only 0.047% and in the kidneys only 0.061% of metallic silver.

As to the circumstances under which excretion takes place we do not yet know any thing positive. The reduced silver deposited in the tissues is never again dissolved and never again excreted. There are older (Orfila, Mayencon, Bergeret, etc.) and more recent observations (Rozsahezgyi) according to which, after the internal use of silver nitrate or silver chloride, silver has been constantly found in the urine. But Jacobi and Gissmann energetically deny the correctness of these observations; these observers were unable even after the most careful observations both on animals and men, to obtain the silver reactions in the urine after the use of any silver preparation, (silver chloride, silver nitrate and solution of the silver chloride in the hyposulphite of soda.)

THERAPEUTIC APPLICATION.

Argentic nitrate is a much used preparation. Its external application is, in some cases, irreplaceable by any other drug; its utility in these cases is undoubted. Its internal application, is, with few exceptions, empirical, and becomes more and more limited, so that to day its utility is doubted in cases in which formerly it was considered highly beneficial.

Argentic nitrate has for a long time been used in many of the convulsive neuroses and most of all in epilepsy. Cases of cure are reported as far back as the beginning of the seventeenth century, and even in the beginning of the present century Portal and Heim were decidedly in favor of this treatment. But since this time confidence in the use of nitrate of silver has steadily diminished, and although the silver nitrate is still used, yet Radcliffe, Reynolds and others state, and their observations have been confirmed by our own experience, that they have seen many epileptics, whose skin has certainly become darkened from the use of silver, but who still retain their malady. This alone would not prove the uselessness of argentic nitrate in epilepsy, since other remedies also often fail in this disease; but according to the large majority of observers, argentic nitrate is even less trustworthy than zinc oxide. We ourselves have never seen any beneficial effect under its use.

Under these circumstances it seems right to neglect the so-called indications for the use of nitrate of silver in this disease, which appear to us to have been founded upon theoretical rather than practical data. It appears but to limit the

use of nitrate of silver to those cases in which the more ordinarily successful remedies have failed. The utility of this drug in chorea and asthma nervosum bronchiale is entirely illusionary.

Lately the silver nitrate has been recommended in tabes dorsalis (Wunderlich, Charcot and Vulpian, Moreau, Friedreich and others) in which it has been said to have produced a considerable improvement, and even curative effect. In the large majority of the cases, however, favorable results are not recorded. We can not doubt its excellent effect in the individual cases reported by the above mentioned excellent observers, and we should the more readily make use of this remedy in tabes when we consider that all other therapeutic resources in this disease are not very effective. There are no special indications, the presence of which in individual cases, would lead us to expect a favorable result, and we shall therefore have to try this drug in each case. Friedreich emphasizes the fact, that we shall have to keep in view the possibility of a nephritis after the long continued use of this drug. We have tried this remedy in other forms of spinal disease (myelitis chronica, sclerosis disseminata) but never with any effect.

Nitrate of silver is often used in diarrhœa but lately it has, with justice, lost much of its popularity. In acute processes accompanied by diarrhœa it is entirely untrustworthy, especially, as we ourselves have observed, in the diarrhœa of children. Rather is it indicated in the chronic and especially in the ulcerative form of diarrhœa. But even here, it is found in practice that the results are so very uncertain, and so slight, that it appears questionable whether these can not be explained as being dependent upon the simultaneous regulation of the diet; the fact that silver nitrate, as such, never reaches the intestine is in favor of such a view. It is only when the salt can be directly applied to the diseased mucous membranes, that we see any result follow its use. This is the case in affections of the rectum and large intestines (as in chronic dysenteric ulcers) here, of course, the drug is not given by the mouth, but by clysters or the Hegar injections.

In affections of the stomach argentic nitrate formerly played an important part, but lately its application in this direction has been very much limited. In the first place, it was given in ulcus ventriculi simplex for two reasons; to cure (heal) the ulcer, and alleviate the severity of the attacks of cardialgia. *Whether the first* of these objects is accomplished is doubtful *and in fact* scarcely possible when we consider how small a

quantity of the remedy is introduced into the stomach and what little chance there is of even the larger portion of it being spread over the ulcer, when we compare its extent with that of the whole mucous membrane of the stomach, apart from the fact that the silver nitrate is generally changed immediately after reaching the stomach into a chemically inactive compound. The later methods of treating gastric ulcer, in which the nitrate of silver takes no part, have produced results which justify this doubt, and under any circumstances prove how well we can get along without it. The good results formerly obtained were probably due to regulation of the diet. Of even less importance is the use of this drug in cardialgia, in which narcotics are far preferable. Besides this nitrate of silver has been given in cardialgia, in which no local disease of the stomach is the exciting cause, as for instance in the gastric pain of pregnant women (often accompanied by vomiting), in that of hysterical patients and enfeebled individuals, in whom even the most easily digested food produces pain in the stomach. In all of these cases the remedy is untrustworthy.

The external use of the nitrate of silver as direct local application is much more extensive. It is used in various affections of the mucous membranes, partly as an astringent, and partly for its caustic effect. Then it is used in simple catarrhs, when these have entered upon a chronic stage or after the severity of the acute symptoms has been diminished. It is thus used in tonsillitis, pharyngitis, laryngitis, rhinitis, conjunctivitis, cystitis and vaginitis; also in contagious urethritis. In all of these cases weak solutions of nitrate of silver have a similar effect to other metallic astringents, and it is partly upon external circumstances that the choice of one or the other depends, as for example the fact that nitrate of silver discolors the clothing. As a rule, however, nitrate of silver in similar solution has a more powerfully astringent effect. In many of these conditions nitrate of silver is used in concentrated solution for its so-called "abortive effect," that is to say to abort newly developing, acute, inflammatory processes; as, for instance, pharyngitis, angina, and more frequently gonorrhœa. The application is sometimes successful, but a very important condition is that the affection be in its earliest stage. Often, however, it fails, especially if applied too late, and in such cases may produce very disagreeable effects, such as urethral strictures, so that altogether it is now considered best not to use it for this purpose. This abortive method has also been used

when a blenorrhœal secretion from any mucous membrane, and especially the urethra, has been brought in contact with the conjunctiva. A solution of nitrate of silver is thus immediately dropped into the conjunctival sac, whence it is disseminated over the whole conjunctiva. A good result is only to be expected when this application follows immediately upon the infection; in these cases the silver nitrate probably acts more by destroying the virus than by any influence upon the inflammatory process. Argentic nitrate is furthermore used as a caustic in croupous and diphtheritic affections. Its utility in these affections has been much over-rated, and it is even probable that burning in these cases does more harm than good. It is certainly true that in diphtheritic angina (for it is in this localization of the process that the caustic is used) argentic nitrate is one of the most useful of all the agents used for destroying the membrane, and that in slighter cases a healing effect follows this destruction; but it must, on the one hand, be remembered that these milder cases get well without the caustic, and that on the other hand the process often attacks the larynx in spite of the caustic, and that notwithstanding the energetic use of the caustic, new deposits develop upon the tonsils; indeed, it is possible that the cauterization favors the spread of the process by depriving healthy portions of the mucous membrane of their epithelium. We must therefore express ourselves decidedly against the use of caustics in angina diphtheritica, and therefore against this use of argentic nitrate.

Furthermore argentic nitrate is used as a caustic in ulcerative processes of mucous membranes, as in ulcers of the larynx, erosions of the cervix uteri, etc. Finally it is used in hyperplastic processes, as in granular conjunctivitis, pannus, etc. There is a difference of opinion as to its utility in urethral strictures. While some praise it, others (Civiale, etc.), are equally warm in its condemnation. At the present time the cauterization of strictures is only seldom attempted.

Nitrate of silver is very frequently used in diseases of the skin and directly underlying tissues. Of the inflammatory affections of the skin, the treatment of paronychia and chilblains by painting with nitrate of silver is most successful; the former of these affections can often be brought to a standstill by the timely application of this remedy. The external use of this substance in erythema is useless; and the attempt to limit the spread of erysipelas by the application of silver nitrate is entirely futile. In burns in which the epidermis has been de-

stroyed, the exposed cutis may be touched with nitrate of silver in order to produce an eschar which will act as a protective to the exposed parts. Experience has, however, not shown that this procedure has any advantage over the painless application of cotton and other similar means. The cauterization of small-pox pustules with a nitrate of silver pencil in order to prevent the formation of disfiguring scars has been shown to be inefficient, as is the case also with the (prophylactic) cauterization of the papules which precede the pustules of small-pox. Of all the other skin diseases there is none in which argentic nitrate is to be preferred to other remedies. For the destruction of tumors, warts, condylomata, etc., the lunar caustic is decidedly inferior to other remedies.

In the treatment of ulcers and sores the use of the nitrate of silver is, under certain circumstances, decidedly beneficial. In the first place it is used to destroy any specific character which may be present in the sore; as for instance in chancres. But it is highly improbable that any favorable result can follow its use in the hard chancre (ulcus durum); that is to say it is not certainly established that cauterization prevents the appearance of secondary manifestations. In the soft chancre (ulcus molle), however, it is different; here it is possible, in fresh sores, to destroy their contagious character and convert them into non-specific simple ulcers. For the cauterization of poisoned wounds (snake bites, bites of mad dogs, etc.), nitrate of silver is entirely inefficient because of the limited character of its effect; the caustic alkalies are here decidedly more effective. In common ulcers, which are "indolent" and which show no tendency to heal, nitrate of silver is useful for stimulating them by the production of a slight inflammatory irritation, and thus causing cicatrization. We must yet mention the application of the argentic nitrate as a hæmostatic, although it is only used as such to stop very slight hæmorrhages, such as those following upon leech bites. The blood must be thoroughly removed, and the point of the nitrate of silver stick applied to the bleeding point. Lately nitrate of silver has been used by Thiersch to destroy malignant growths, such as carcinomata. This observer repeatedly injected weak solutions of argentic nitrate (1 : 2,000–3,000), followed by injections of solutions of sodium chloride (1–1,000–1,500) into the tumors, and found that without any signs of inflammation following the diseased tissues were disintegrated, and disappeared. Further observation has confirmed these results, but they were *found to depend mostly* upon a separation of the diseased

growth, owing to a destructive inflammatory process, which was certainly not in accordance with the original intention.

Dosage and Preparations.—Argentum nitricum crystallisatum, internally from 0.005–0.03 per dose (ad 0.03 per dose! ad 0.2 per day!) in solution; to be dispensed in a dark bottle. In pill* (with argilla); pastilles cannot be kept on account of the rapid decomposition. Externally the nitrate of silver is used either in substance (for which purpose it should be held in a caustic holder, or the hands protected in some other way), or it can be used in solutions of different strength; for cauterization, from 2–10 per cent. As an eye-wash only the weakest solutions, and as an astringent we use from ½–5 per cent. solutions, according to the location of the application, the weakest being used for the conjunctiva and external auditory canal. As menstruum we must use either distilled water or the purest of glycerine. The ointment, which is very little used, is only of slight utility. We use from 0 2–0.5 of silver to 10.0 of simple ointment.

2. Argentum nitricum fusum, used like the crystallized.

3. Argent nit. cum kali nitrico, in the proportion of 1 of the first to 2 of the second; of stronger consistency than the ordinary nitrate of silver stick, and a less energetic caustic.

APPENDIX.

Arg. foliatum—silver leaf; used for covering disagreeably tasting pills, the pill mass of which has no chemical effect upon silver.

Treatment of Silver Poisoning.—In poisoning due to argentic nitrate (which alone we shall consider), we administer, as after other metallic poisons, milk and albumen, in order to dissolve the pieces of nitrate of silver which may have gained access to the stomach, (as for instance by being broken off in using the argent. nit. for cauterizing the throat) and to prevent its caustic action upon any one spot in the stomach. In addition to this, however, we must immediately administer common salt in solution, in quantity sufficient to form a harmless silver chloride, although this salt is soluble in the gastric juice. For subacute and chronic silver poisoning there is no rational treatment.

COPPER AND ZINC.

Both of these metals are so similar to each other in their physiological and therapeutic action that we could almost consider them under one head, if the copper had not in general a stronger effect than the similar zinc salt. Cadmium, which physiologically and chemically is analogous to zinc, is scarcely used at all; nor is there any reason why this metal should be used, and for this reason we shall consider this short notice of it sufficient.

These metals are allied to lead in so far that their preparations have a similar contractile effect upon the vessels, and diminish the quantity of the secretions; lead, on the other hand, *does not act* as an emetic as do salts of these metals.

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*Gum arabic is a good excipient. (Translator.)

COPPER—CUPRUM.

Since all the compounds of copper, whether given in large doses or in small doses long continued, develop the same physiological action, we shall first consider them in common.

PHYSIOLOGICAL ACTION.

All of the soluble copper salts, like those of the other metals, enter into chemical combination with the albuminoid bodies. Upon the copper albuminate thus formed a large part of the physiological action is thought to depend.

Local Action.—Since these salts have no effect upon the epidermis they have no effect upon the unbroken skin, and when thus applied are not absorbed.

They do, however, as already stated, enter into combination with the albuminoid bodies of the secretions and mucous membranes, and thus exert an action similar to the lead preparations in dilute solutions, that is to say an astringent effect upon cells and bloodvessels, diminishing the amount of the secretions and antagonizing the inflammatory process. In concentrated solution they have a caustic effect, which is stronger than that of lead and zinc. Upon *suppurating surfaces* copper solutions, like those of lead, have the effect of diminishing the secretion; the affected surface becomes drier and heals more readily. Internally administered, small dilute quantities (0.03 grms.) produce, in addition to the metallic taste, digestive disturbances and constipation, as do the lead salts.

Larger quantities (0.2 grms. on an average) cause nausea, vomiting and diarrhœa.

Since the direct injection of this drug into the blood of dogs caused no vomiting, while the introduction of even small doses by the stomach did cause vomiting (Dalitzky, Harnack), we would consider it very probable that the emesis is the reflex result of the irritation of the nerves of the mucous membrane of the stomach.

Very large quantities (1.0) produce, in the same way as the other metals, severe inflammation of the gastro-intestinal mucous membrane with all the characteristic symptoms, such as severe colicky pains, vomiting and purging.

Absorption.—It has been positively determined that solutions of copper are *readily* absorbed into the blood from the *stomach and intestines.* Indeed, so frequently was copper

found in the human organism, that it was concluded that this metal is a normal component of the human body. But Lossen showed that copper was only found after the eating of food containing copper (as, for instance, food which had been cooked in copper vessels). If this has not been the case we do not find copper in any part of the organism.

There is no longer any doubt that general symptoms of poisoning can result from the absorption of copper. But these are generally seen only after the use of small doses, for when larger amounts are introduced into the stomach the greater part of them is immediately vomited.

The general effect of copper is, as Orfila, Blake and Neebe found, especially exerted upon the muscles of the trunk and heart. Harnack obtained the following results by the introduction into the body of a double salt, the tartrate of copper oxide and sodium, this salt being chosen because it does not produce clotting of the blood in the vessels, which would otherwise introduce a foreign element into the symptomatology. In frogs the subcutaneous injection of 0.0005 to 0.007 grm. (calculated upon the proportion of copper oxide) was followed in a few hours by muscular paralysis preceded by trembling. Muscular irritability was entirely lost without *rigor mortis* setting in. In warm-blooded animals there is unsteadiness in gait, weakness and finally complete paralysis. The pulsations of the heart and respiratory movements become extraordinarily weak and slow, as if about to cease entirely; the pupils become dilated. Although direct muscular irritability is destroyed, yet sensation and the functions of the central nervous system remain undiminished until death. Rabbits die after the subcutaneous injection of 0.5 grm., dogs from 0.4 grm.; but when injected directly into the blood, the former die from 0.01 to 0.015 grm., the latter from 0.025 grm. of the copper oxide. It is a curious fact that whether the double salt or the albuminate were used, it was observed that even when injected directly into the vein (jugular vein) it was hours before the physiological effect manifested itself, which seems to prove that the metal is for a time detained in the blood, reaching the locality upon which it exerts its specific action only after the lapse of some time.

Chronic copper poisoning in man, as, for instance, those who work in copper, although never clearly demonstrated, cannot positively be said never to occur. Many of the symptoms, such as catarrh of the various mucous membranes of the air passages, depend rather upon the irritation produced by dust which is

inhaled, than upon any absorption of copper into the system. Other symptoms ascribed to copper poisoning, such as the various neuralgias, muscular cramps, trembling, attacks of colic and general wasting, generally occur in workmen who have at the same time been exposed to lead influence, and it is therefore at least highly probable that they are due to the lead and not the copper. The green color of the hair and perspiration, so often observed in workmen on copper, can be much more readily explained by a mechanical intermingling of the copper with the fatty matter of the skin and hair, forming a salt of copper with the fatty acid, than that the copper has been internally absorbed. The purple red (Corrigan) or green color (Clapton) of the gums can be explained in the same way. Bucquoy finds fault with the term copper line (kupfersaum) because the discoloration is not, as in lead, upon the gums, but a bluish-green discoloration at the base of the teeth, while the gums are reddened, owing to a chronic inflammation. We have left, then, only certain vague symptoms, such as diminution of the appetite and digestive power, frequent diarrhœa, wasting, etc., which may just as well be the results of the poor diet and hygienic surroundings of the workmen as of the copper. When we consider the characteristic symptoms produced by the easily absorbed copper compounds (see above) we cannot believe that chronic copper poisoning, if there were such a condition, would not give well-marked symptoms. And since such symptoms have not hitherto been noticed, it would appear that chronic copper poisoning does not take place, perhaps because the copper salts to which workmen and others are exposed are of such a nature that they cannot be absorbed.

According to Galippe, Burg and Ducom animals can take large amounts of copper and copper oxide for a long time without any injurious effect; even the soluble copper salts can be taken in gradually increasing doses (from 0.1 to 1.0 grm.) for months, if introduced into the alimentary canal mixed with the forage. A dog to whom even as much as 4.0 grms. of the copper salt are daily administered, and who vomits one or two hours after the meal and thus rejects a large part of the copper salt, is not affected in his health. It is only after a long time that diarrhœa sets in and the dog grows lean rapidly and often dies.

The excretion of copper seems to take place principally through the bile and to a slight extent through the urine.

The disinfecting power of the copper salts is not very great;

for it is not until a concentration of 1–130 has been reached that the development of bacteria is prevented.

COPPER SULPHATE—CUPRUM SULPHURICUM PURUM—COPPER VITRIOL—(BLUE VITRIOL).

Cupric sulphate SO_4Cu+5H_2O presents large blue crystals soluble in 2½ parts of cold and ½ part of boiling water. The crystals effloresce in the air.

THERAPEUTIC APPLICATION.

The internal use of blue vitriol is very limited. Decided benefit is only to be expected from it when used as an emetic. It has several advantages over the commonly used emetics. In the first place its effect is almost certain to follow, and can be used in cases in which ipecac and tartar emetic are denied us. But this energetic action is exaggerated, for common experience teaches that even cupric sulphate often deserts us.

Blue vitriol has the advantage over tartar emetic in that the resulting collapse is much slighter and the preceding nausea shorter and less intense. We must be careful, however, in its application if there be a tendency to diarrhœa. In narcotic poisoning it is much used, but has been most recommended in croupous laryngitis and diphtheria. The just mentioned advantages of this salt as an emetic have made it a favorite one to use in those affections in which the patients are weak and deteriorated, and can therefore ill afford to be thrown into a more intense asthenia by long continuing nausea, or the collapse following the use of tartar emetic. But that the salt exercises any influence upon the process itself, as some physicians have thought, has not been proven, and its continuous use in broken doses is not only superfluous, but even injurious on account of its effect upon the gastric mucous membrane and the digestive process. Blue vitriol is furthermore recommended in phosphorus poisoning not only as an emetic, but also in divided doses as an antidote (Bamberger, Eulenberg and Landois). This application is based upon the fact that phosphorus, even in the form of vapor, reduces the copper sulphate, metallic sulphur being deposited upon the phosphorus and preventing its action.

Other conditions in which this remedy might be useful have not been determined.

Externally copper sulphate is much used under the same circumstances as the zinc sulphate. We therefore refer to what

is said under the head of the latter salt. These salts present no decided difference in their therapeutic action; in most cases it is more a matter of taste as to which shall be chosen.

In trachoma of the conjunctiva, however, we use sulphate of copper in crystalline form as a direct application, because, of all the analogous salts, this, together with the nitrate of silver, are of such a physical nature that they can be used for "touching up" the conjunctiva; for instance, in the case of copper sulphate we have a broad and smooth surface which adapts itself readily to this purpose.

Dosage.—Cuprum sulphuricum purum internally from 0.01 to 0.1 per dose (ad. 0.1 pro dosi! ad. 0.4 pro die!). As an emetic from 0.1 to 0.4; for children, 0.05 to 0.1 (ad. 1.0 refracta dosi!), in solution, powder or pill. Externally as a mild caustic in substance. Large crystals should be selected for this purpose, which may be either pointed or flattened according to the necessities of the case. When a crystal is to be applied to the conjunctiva, the raw edges must be ground off, and the deliquesced portion separated by washing in water.

As an injection, $\frac{1}{10}$–1 per cent.; as a lotion for painting, 1–10 per cent.; and as an eye wash, $\frac{1}{10}$–1 per cent. solutions.

2. Cuprum sulphuricum crudum—superfluous.

APPENDIX.

Acetate of copper, cuprum aceticum, verdigris, (aerugo), usually formed on the surface of copper plates, is a mixture of several basis salts.

The salt here mentioned is the neutral copper acetate $Cu(OCO\ CH_3)_2 + 5H_2O$ which is produced by the solution of copper oxide in acetic acid, and crystallizes sometimes in blue and sometimes in dark green crystals, which are not easily soluble in water. Its physiological action is the same as that of the copper sulphate. Therapeutically this preparation is of no importance.

Ceratum æruginis, 1 part to 12 of cera flava, 6 parts of res. pini and 4 parts of terebinthina.

Cuprammonium sulphate, cuprum sulphuricum ammoniatum $So_4Cu + NH_3 + H_2O$. A blue nauseous crystalline powder which readily undergoes decomposition.

It is said to be capable of dissolving the epidermis, etc., otherwise its action resembles that of the substances into which it is so easily decomposed, namely, copper sulphate and ammonia.

Cuprammonium was formerly much given in the "spasmodic" neuroses, such as chorea, asthma, etc., but most of all in epilepsy. It is one of the oldest of the metallic anti-epileptic remedies, having been used even by Paracelsus and Helmont. More recently it has been recommended by Jos. Frank. The statement of some observers that its administration is accompanied by danger (Portland) is exaggerated.

The statements of others (Radcliffe, Reynolds) who affirm that it exerts no anti-epileptic effect at all are opposed to the positive affirmation of others; but even the latter speak only of occasional benefit resulting from the use of cuprammonium. We ourselves, however, have obtained as little benefit from the use of this salt in epilepsy as Reynolds has.

From 0.01 to 0.05 several times a day (ad. 0.1 pro dosi; ad. 0.4 pro die).

* Cuprammonium chloride, cuprum chloratum ammoniacale, colorless, easily soluble and decomposable crystals, having no physiological or therapeutic importance.

Copper alum, cuprum aluminatum (lapis divinus s. ophthalmicus), obtained by melting together 16 parts each of cuprum sulphuricum, kalium nitricum and alum and 1 part of camphor, is a light blue greenish mass, which can be cast in sticks like those of argentic nitrate. Copper alum, when applied locally to mucous membranes and granulating surfaces has an effect analogous to that of blue vitriol (only milder in degree), that is to say, it acts as an irritant and astringent. It is applied, like that latter salt, in external conditions. In substance or solution (0.01–1.0 to 10.0).

Cuprum oxidatum, *carbonicum, *nitricum, *chloratum and *iodatum have an effect very similar to that of the other preparations, and are therefore superfluous.

* Cuprum perchloratum, because it gives off chlorine when heated, has been recommended as a disinfectant.

Treatment of Acute Copper Poisoning.—Vomiting need not be produced, since this follows the administration of poisonous doses of copper sulphate or acetate. Of the many antidotes recommended only a few have been practically used. Under any circumstances albumen or milk should be given, and magnesia usta can also be administered. Sugar has been warmly recommended, but its utility has not yet been established. There are also other antidotes, such as potassium ferrocyanide, iron powder, and a mixture of iron filings and flowers of sulphur in syrup.

ZINC—ZINCUM.

Since the soluble zinc compounds have an exactly similar but rather weaker action than copper compounds, we can be very brief in their consideration.

But while none of the compounds of copper, which are insoluble in water, are used therapeutically, we have the oxide of zinc, which is insoluble in water to consider, because it is practically used. But even this compound has a similar although weaker action to that of the soluble salts, and it must therefore be administered in larger doses. On the other hand the easily diffusible zinc chloride has a much more intense action upon the tissues than any of the copper preparations, and it must therefore be administered in much greater dilution.

We can therefore consider the physiological action of the zinc preparations in general, apart from their dosage, in the introduction, especially since the chloride of zinc, which has a strong effect, is not used internally, but only as a caustic.

PHYSIOLOGICAL ACTION.

Zinc salts enter into combination with albumen and there- ... e *the copper* salts, they have an astringent effect upon

the tissues and vessels. In smaller doses they cause vomiting and diarrhœa, in larger and concentrated doses, gastro-enteritis.

As one of the acute general effects of the absorption of comparatively small doses, (of zinc acetate for example), we have according to Meihuizen a diminution of the reflex irritability; according to Michaelis, on the contrary, even moderate doses are followed by convulsive stretching of the limbs, and general convulsions. Letheby, Blake, Falck and Harnack on the other hand found that the zinc salts, like those of copper, only exert an effect upon the muscles of the body and heart, producing death by paralysis of the heart and respiratory muscles. No direct effect upon the central nervous system is observed. Sensibility is according to Blake uninfluenced.

Chronic zinc poisoning.—Although until recent times no well observed cases of chronic zinc poisoning had been seen, and its occurrence had been doubted, yet in the present year Schlokow has observed many workmen of zinc foundries who were affected by a peculiar disease, which seemed to be the result of chronic zinc poisoning. The well marked and characteristic symptoms of all of these cases were as follows: At first symptoms of irritation in the sensitive nerves of the skin; later on anæsthesia and analgesia set in, also a feeling of a band around the body, increase of reflex irritability, and convulsive muscular twitchings, followed later on by an almost paralytic condition of the muscles, diminished muscular sense, and disturbances in co-ordinate movements. The character, and bilateral occurrence of these symptoms point according to Schlokow, to inflammation of the spinal cord, in the region of the anterior and lateral columns. Although at first, the more serious cases of this affection remind one of patients suffering from tabes dorsalis (gray degeneration of the post. columns.) But many of the symptoms are entirely different from those in this disease, such as the presence of tendon reflex, the absence of symptons of bladder and rectal paresis, and of severe neuralgic pains, inequality of the pupils, affections of the ocular muscles and serious visual disturbances, and lastly the paralytic and ataxic walk. From sclerosis of the lateral columns chronic zinc poisoning is also distinguished; as we do not find in the latter, the stiffness and contractures existing in the former. Zinc poisoning is distinguished from lead poisoning by its late occurrence (10 years after the workman has been employed at zinc) the absence of colic and constipation; and furthermore in that the paralysis is at first almost entirely limited

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to the lower extremities (while in lead it first affects the upper) the upper extremities being involved later on. It is also distinguished from lead palsy, in that the latter is never preceded by hyperæsthesia or increased reflex irritability; and finally in the fact that the muscles paralyzed by zinc palsy remain well nourished and retain their irritability for a much longer time than those affected by lead. We must remember, however, that our knowledge is still incomplete in anatomical and chemical observations. Zinc was never found in the urine of these patients.

Popoff observed in workmen, who worked the whole day in a zinc atmosphere, severe headache, a feeling of chilliness, convulsive movements of the extremities, especially of the muscles of the calf, severe nausea and vomiting, purging (often choleriform) and severe attacks of colic. Even after months of freedom from the inhalation of the continued zinc atmosphere, zinc could still be found in the urine.

Upon the lowest organisms the zinc salts have no particular effect. The development of bacteria for instance, is not suspended until a concentration of 1 to 50 of the zinc sulphate has been reached.

I.—ZINC OXIDE—ZINCUM OXIDATUM PURUM.

We have an impure zinc oxide for external application, and the pure zinc oxide (mentioned in the caption), ZnO which is a soft white powder, turning yellow when exposed to heat, insoluble in water, but soluble in acids.

PHYSIOLOGICAL ACTION.

The physiological effect of this salt is only different from the general effect of all the zinc compounds, as given in the introduction, in the fact that it is insoluble in water. It is soluble, however, in the gastric juice, and thus produces all of the general effects of the zinc compounds, upon the stomach and intestines; but larger quantities and longer continued administration is necessary to produce these effects. The formerly supposed narcotic action of the drug, an effect held to be similar to that of opium, has shown itself to be without foundation.

THERAPEUTIC APPLICATION.

The application of the zinc oxide is purely empirical. The only use which is derived from its physiological action, is its use as an emetic, and even for this purpose it is scarcely ever employed.

This preparation is very much used in the motor neuroses, especially in the various convulsive affections, such as epilepsy. Gaub was the first to use the zinc oxide in this disease, but more recently Herpin has been very warm in its recommendation; he pretends to have cured 28 out of 42 cases. A careful analysis of these cases will, as Radcliffe has shown, reduce this number; but to deny any curative effect to zinc is not correct, for a recent examination of these cases by Voisin has shown, that many of the patients have had no attack for 10 years. The views of different observers concerning this question differ very much. Some who pretend to have used the remedy according to the directions of Herpin, say they saw no effect from its use; among these are Moreau, Delasiauve and Radcliffe. Others, as for instance Graves, consider its power limited to the production of a longer interval between the attacks and not to a cure. More accurate indications for its use, as well as in what cases of this affection in adults we may expect a good result, we have no means of stating. The remedy must therefore be used in an entirely empirical manner. But a consideration of the literature of the subject does seem to warrant one indication for the use of the zinc oxide, namely in the epilepsy of children. Herpin himself, in his later reports, states that the zinc oxide very often disappoints us in adults, while it is very well fitted for children. Similar statements are made by Brachet, Joseph, Frank and others. But we must remember that the convulsions of the dentition period are often "cured" without any medicine. We ourselves have often seen a curative effect follow the use of the pulvus antiepilepticus, in which zinc is the principal constituent, when administered to inveterate epileptics, after the potassium bromide has been administered without any useful result. The value of this remedy in chorea, pertussis and other neuroses is even less positive than in epilepsy. Recently Butlin, for instance, has recommended the sulphate of zinc very highly in chorea, but here again without indicating the conditions in which it should be preferred to other remedies. Herpin increased the dose up to a 1.0 grm. daily, continuing this dose for weeks. In neuralgias this remedy is particularly recommended by Valleix, in combination with hyoscyamus, in the form of Meglin's pills. Concerning its value, see hyoscyamus.

During the last few years, French writers, following the lead of Gubler, have recommended the zinc oxide as a remedy for chronic or at least not recent diarrhœa.

An accurate particularization of the cases is not given. 3.5

grms. of zinc with 0.5 of sod. bicarb. divided into 4 doses, are to be given daily. For the sweats of phthisis it is, like lead acetate, now very little used in Germany, although still extensively used in England.

Externally the zinc oxide is a frequently used preparation, as a dressing for suppurating wounds, and in the form of zinc salve it is used to cover superficial loss of skin, as in intertrigo, blistered surfaces, etc. Secretions are slightly diminished by its use.

Dosage and Preparations.—Internally the zincum oxidatum purum is to be preferred to the venale; from 0.05–0.5 per dose (3.0 per day) in powder or pill. Externally it is used as a salve or liniment. (1 to 5–10).

Unguentum zinci.—1 part of zinc and 9 of ung. rosat.

2. ZINC SULPHATE--ZINCUM SULPHURICUM PURUM.

ZINC VITRIOL (WHITE VITRIOL.)

Zinc sulphate presents colorless, efflorescent crystals, which are soluble in water.

THERAPEUTIC APPLICATION.

Zinc sulphate is used internally in the same neuroses in which we use the zinc oxide, and some authors, such as Schroff and Tuerk, even prefer it to the latter. Experience, however, teaches that the results are altogether just as uncertain as those derived from zinc oxide; and since we do not know of any indications for its use, and since in addition the long-continued use of the drug produces digestive disturbances, it is perhaps best to exclude the drug from internal use for this purpose. Furthermore, this preparation has been used as an astringent in a number of conditions, especially in an abnormal condition of the secretions of the mucous membranes, in bronchial catarrh, intestinal catarrh, etc. That it does act as an astringent in intestinal catarrh is true, but for this purpose we have other more energetic remedies, which have not the disadvantages of zinc sulphate. Finally, zinc sulphate is used as an *emetic* in cramp and poisoning by narcotic substances. It is, indeed, an active emetic, but in the cases in which it is generally used, that is in cramp, we should prefer the copper sulphate, because the irritative effects of the latter upon the mucous membrane of the stomach are not so intense. One advantage of the zinc sulphate over the ordinary emetics, ipecacuanha and tartar emetic, is that the antecedent nausea is of
·r duration.

Externally the zinc sulphate is much more frequently used than internally. By combining with the albuminates of the secretions and tissues, it acts like zinc oxide, as an astringent and drying agent. Its astringent action can probably be accounted for partly by its direct influence upon the vessels, which it causes to contract. It is a very popular application in catarrhs, especially in gonorrhœa. Zinc solutions (to which some tincture of opium is added) are the most useful and effective injections in this affection. The weak injections of zinc can be applied in any stage of the gonorrhœa, even in the acute stage; under their use the gonorrhœa is sometimes cured in a few days. They are least effective in gleet. In simple catarrhal conjunctivitis also zinc sulphate is preferred to the other metallic astringents, not so much because it is more effective, but because it does not possess as many disadvantages. Drops of zinc solutions are used in the secondary stages of the ordinary syndesmitis; but here, even more than in gonorrhœa, we must be careful that all acute inflammatory symptoms are passed. In specific blenorrhœa of the conjunctiva, zinc is inferior to silver nitrate. Zinc sulphate is also frequently used in catarrhal inflammations of the genital passages in women; it is also used as lotion to suppurating surfaces. Finally, we should mention that very dilute solutions of zinc sulphate are used as disinfectant wash for linen, etc.

Dosage.—Zinc. sulph. pur. Internally, for long continued use from 0.01–0.05 (ad 0.05 pro dosi, ad 0.5 pro die) in pill or solution. As an emetic, from 0.3–0.6–1.2 (ad. 1.2 pro dosi) in solution. Externally we generally use as astringents 1-5 % watery solution (with tinctura thebaica). As lotion for suppurating surfaces 1–3 % solution; as an ointment, 1.0 to 15.0 of simple ointment. As an eye powder, 1 part to 5 parts of sugar.

The lactate, acetate and valerianate of zinc are entirely superfluous preparations. The maximum dose of zinc lactate and valerianate is for each 0.05 pro dosi ! ad 0.3 pro die !

3. ZINC CHLORIDE.—ZINCUM CHLORATUM.

The chloride of zinc is obtained free from water by burning zinc in chlorine gas. In this form it is a white, easily deliquescent and soluble mass. In concentrated solutions octohedral crystals of $ZnCl_2+H_2O$ are deposited.

PHYSIOLOGICAL ACTION.

In small quantities and strong dilution it acts very much like the other zinc compounds. It is only used as a caustic, because owing to its ready diffusibility and its affinity for albumen, it destroys most tissues, its effect being sharply limited to

the point of application but cauterizing very deeply. Very intense pain is thus produced, the eschar is generally thrown off in about 8 days by a reactionary inflammation, a healthy and rapidly cicatrizing surface being left.

THERAPEUTIC APPLICATION.

The internal use of this preparation should be discontinued on account of its danger, and because it is in no way superior to the other zinc preparations.

Externally zinc chloride has been used as an astringent preparation, but for this purpose we have better compounds. But as a thorough, deeply destructive caustic it can be used in those conditions which we shall formulate under the head of arsenic (to which we refer). Koebner recommends this preparation in the form of the chloride of zinc pencil, which is a mixture of chloride of zinc and potassium nitate (5 to 1). The caustic effect is about a mean between that of caustic potash and nitrate of silver, but the effect is more easily localized than when potash is used, while the eschar that is left is very much like that from silver nitrate. The chloride of zinc sticks can be used for cauterizing syphilitic and non-specific sores, as well as for the removal of small growths. Koenig prefers the chloride of zinc to other caustics in hospital gangrene, because it can be used for impregnating cotton which can be inserted into every portion of the inflamed wound, and after being left for 8 or 10 minutes produces an energetic and yet local effect.

In the Lister method of treatment of wounds the chloride of zinc is sometimes used. An 8 % solution is used to render aseptic wounds, sores and fistulæ. And also in certain localities where, as for instance the perineum and the region around the anus, the usual Lister manipulations and bandages cannot be applied.

Dosage.—Zincum chloratum. Internally from 0.005–0.015, 2–3 times a day in solution (ad 0.015 pro dosi ! ad 0.1 pro die !) Externally as a lotion in 2–3 % solution. For caustic purposes we should select the paste. Canquoin has proposed several strengths; 2 parts of flour and 1 part of zinc chloride or 3 to 1 or 4 to 1. But little water should be added. and the paste should be applied the more thickly the deeper the effect required. Landolfi's (very painful) caustic paste, contains in addition to the zinc chloride, antimonious chloride and chloride of bromine as active ingredients.

APPENDIX.

Treatment of Zinc Poisoning.—Zinc poisoning is generally caused, save in some exceptional cases, by zinc vitriol or zinc chloride, and since vomiting is the natural effect of this drug, we need administer no emetic; but only milk and albumen and the carbonates and phosphates as harmless antidotes.

IRON—FERRUM.

Iron differs from the other heavy metals as far as its position in the animal organism is concerned, in that it is the only metal which is naturally taken into the system during life in small daily doses, producing no injurious effect upon the organism, nor any chronic poisoning. It is furthermore the only metal which is the normal component of the organism, and which plays an extraordinarily important part in the processes of life.

PHYSIOLOGICAL IMPORTANCE AND ACTION.

Iron is an important component of the living organism ; a man 70 kilograms in weight has on an average 3.07 grams of iron in his system (Gorup-Besanez) ; all of it is derived from the food which is introduced into the body, excepting a small amount present in the hæmoglobin at birth. For this reason it is interesting to study the percentage of iron present in principal articles of food. Boussingault in his observations found that 100 grms. (including the water) of :

Beef.................	contains	0.0048	Grms.	of Iron.
Veal.................	"	0.0027	"	"
Fish.................	"	0.0042	"	"
Cow's milk...........	"	0.0018	"	"
Hen's egg............	"	0.0057	"	"
White wheat bread...	"	0.0048	"	"
Rice.................	"	0.0015	"	"
Beans................	"	0.0074	"	"
Lentils..............	"	0.0083	"	"
Potatoes.............	"	0.0016	"	"
Oats.................	"	0.0131	"	"
Green cabbage leaves	"	0.0039	"	"
100 CM. of				
Red wine (Beaujolais)	"	0.000109	"	"
White wine (Elsass)..	"	0.000076	"	"
Beer.................	"	0.000040	"	"

From this and other tables Boussingault determines the amount of iron taken in the ordinary diet of men and animals and finds that in the daily rations of French soldiers 0.00661–0.0780 grms. are taken. An Irish laborer takes 0.0912 grms., a horse 1.0166–1.5612 grms. of iron.

So that on an average 0.05 *grms. of iron taken with the food suffice to satisfy the needs of the human organism.*

ABSORPTION AND EXCRETION OF IRON.

Absorption of iron into the body and its local effect upon the digestive canal.—No iron can be absorbed by the unbroken skin, so that improvement of patients after the use of iron baths is not due to the absorption of iron. It can, however, be absorbed through wounds and sores. When injected into the areolar tissue the easily soluble and weak iron salts, as for instance, citrate of iron, and the weak alkaline reacting albuminate and peptonate of iron, are rapidly absorbed, and appear in the urine after the lapse of an hour. The strong styptic salts, as for instance, the ferric chloride, destroy tissues and can not be absorbed into the blood.

All of the soluble iron compounds produce a puckery metallic taste in the mouth, where they enter into combination with the albuminoid bodies of the mucous membrane of the mouth and the superficial terminations of the nerves of taste. The intensity of the ferric taste varies in different preparations, and the strength of solution which can be thus appreciated varies from 1 : 2000–9999. Iron albuminate leaves no taste, because the affinity of the iron is already satisfied. The black discoloration of the teeth which occurs after the soluble iron salts have been taken for some time is due in some cases to the formation of the iron sulphide, in others to the formation of the iron tannate. Small quantities of iron are absorbed even by the mucous membrane of the mouth.

In the stomach the insoluble iron preparations are partly dissolved by the action of the gastric juice. Metallic iron is converted by the decomposition of water and the liberation of hydrogen (hence the gaseous eructation), into ferrous and ferric oxide, with which the acids of the stomach unite to form salts. Indeed, all of the iron preparations, even those which are with difficulty soluble, are converted in the stomach into iron chloride, from which it follows that it is of little importance what preparation of iron is administered. In the acid contents of the stomach this iron chloride exists beside acid albumen and peptone. Inasmuch as iron never enters into combination with albuminoids or peptones, in acid solution, the mucus membrane of the stomach is not affected by the iron salt. The absorption of this iron chloride into the blood takes place very rapidly, where it enters into combination with the albumen *which is present*, and these two, in addition to the free alkali, *which is also present*, combine to form the soluble alkaline iron

albuminate, and under this form it circulates in the blood until it is taken up by the hæmoglobin (Scherpf).

The portion of iron not absorbed in the stomach, reaches the portion of the intestine in which the contents have an alkaline reaction, and is thus converted into the alkaline iron albuminate and peptonate and is thus absorbed (Scherpf).

The digestive disturbances which sometimes result after the long continued use of iron, seem to occur when not sufficient albumen is taken simultaneously with the iron, and when too little or no gastric juice is secreted. To prevent this then it would seem to be best to administer with the iron a diet rich in albumen and hydrochloric acid.

Large and concentrated doses of iron cause gastro-enteritis; (pressure at the pit of the stomach, abdominal pains and diarrhœa) when the iron is compelled to satisfy its affinity from the albuminoid bodies of the gastro-intestinal mucous membrane.

From the fact that after the administration of small or large amounts of iron almost an equal amount is found in the stool, it was concluded that almost no iron is absorbed from the stomach and intestines. But this conclusion is not warranted for, as we shall soon show, considerable quantities of iron are excreted with the bile. The deficiency thus produced can only be made good by absorption of iron which has been introduced from without. The observations of Wild concerning the absorption and excretion of iron in the course of the intestinal canal, give us a very interesting picture. This observer allowed sheep to feed upon hay, which contained 0.236% of iron oxide, for ten days, and found that during its course through the gastro-intestinal canal, the percentage of iron in the food and and fæcal mass changed in the following manner at different portions of the gastro-intestinal canal:

Hay.	Stomach.	Paunch.	Rennet.	Small Intestine.	Cæcum.	Large intestine.	Rectum.
0.236%	0.058%	0.070%	0.111%	0.138%	0.197%	0.170%	0.217%

This proves that a considerable proportion (almost half of that introduced) of the iron is absorbed in the stomach, but rapidly excreted by the intestinal secretions, so that a *very active absorption and excretion of iron must be going on.* Indeed, even in the lower divisions of the stomach an increase in the quantity of iron appears, so that not only is iron absorbed in the stomach but it is also excreted by the gastric juices.

Excretion of the Iron from the Organism.—The fact which we have already mentioned in contradistinction to the com-

monly received opinion, namely, that large quantities of iron are constantly taken up into the blood, and that the transformation of iron in the body is a very considerable one, furthermore appears from the fact that iron appears in all of the secretions, and leaves the body by many channels. Although in many of the excretions only traces are found, yet in the course of the day they must amount to pretty large quantities. Constant excretion can only take place in the normal organism, when there is a continuous absorption; otherwise the total proportion of iron in the system would be diminished and disease would ensue.

Very small quantities of iron are found in the perspiration, saliva, gastric and pancreatic juices, mucus (of all the mucous membranes) and pus. In the milk of goats and women Liebreich found 0.01 per cent. of iron; this quantity is increased, however, if iron be internally administered.

The urine also contains only small quantities of iron. In Scherer's "urine pigment" there is a material soluble in ether, Harley's urohæmatin, which generally contains iron. Magnier found in 1 liter of urine 0.007 of iron. The average daily quantity of iron in the urine (1500 ccm. daily) is 0.01 grms. (Hamburger).

According to Hamburger, the use of the iron preparations does not sensibly increase the proportion of iron excreted in the urine. Since the iron in the urine does not respond to the iron reagents (ammonium sulphide), he believes that it is not excreted as such, but as an organic body containing iron. Mayer, indeed, doubts whether the iron in the urine originates from the kidneys. It may just as well have been excreted from the mucous membrane of the urinary passages.

The bile is, according to all investigations, the fluid which takes the largest amount of iron from the blood. In 100 parts of fresh human and animal bile there are between 0.004 and 0.0068 parts of iron (Young, Hoppe-Seyler, Kunkel).

The amount of iron daily excreted by the bile was found by Kunkel to be 0.004–0.006 in a dog with a biliary fistula weighing 4 kilograms. In man the amount of iron daily excreted with the bile has not yet been determined. However, if J. Ranke's estimate of 600 ccm. per day for an adult, be taken in conjunction with Young's average percentage of iron in the bile, we find this to be about 0.0408 grms. The source of the iron thus contained in the bilrubin is, according to Hoppe-Seyler, *Maly and Jaffe,* the decomposition of hæmatin.

Since in 100 parts of biliary coloring matter there are only

1.5 parts of iron, and in 100 parts of hæmatin 9.79 parts of iron, Kunkel concludes that when hæmatin is decomposed a large portion, rich in iron, is retained in the blood, while a small portion is excreted in the coloring matter of the bile. Kunkel thinks that the most probable form of the iron in the blood is the ferrous phosphite.

The largest part of the iron contained in the fæces originates in the non-absorbed portion of the iron in the food, which passes through the intestinal canal; but partly also from the iron present in the bile, pancreatic juice and mucus of the intestinal mucous membrane. This is converted into iron sulphide which gives the black color to the fæces. According to Fleitmann the daily amount of iron thus found in the fæces amounts on an average to 0.038 grms. Bidder and Schmidt found even in starving animals a large percentage of iron in the fæces, 6–10 times as much as in the urine. From this they concluded that the intestinal canal was the chief channel of excretion for the iron.

If we take in consideration the amount of iron excreted by the saliva, mucus, fæces and urine, and worn off with the hair and epidermal scales, it will appear that as much iron is daily excreted as is absorbed, namely, 0.05 grms.

The Function of Iron in the Blood.—All observations have demonstrated with the greatest certainty, that the functional activity of iron in the body takes place in the blood and not in the organs. And, moreover, it has been shown that iron is the most important constituent of the blood, and that blood cannot be formed without it.

The iron of the blood is not combined with the serum but chemically with the hæmoglobin. Hæmoglobin of different species of animals has a distinctive composition, so that in the same species each molecule of hæmoglobin contains equal amounts of iron. Knowing, therefore, the percentage of iron contained in the blood of a particular animal, we can calculate the amount of hæmoglobin in the blood or *vice versa*. The amount of iron contained in the blood is therefore proportionate to the amount of hæmoglobin. We cannot give the physiological action of iron apart from that of hæmoglobin.

Pure hæmoglobin crystals of various animals have, according to Hoppe-Seyler, the following composition:

Oxyhæmoglobin crystals in	Water of crystalization.	In the residue dried at over 100° was found.						
		C	H	N	O	S	Fe	P_2O_5
Dogs........	3-4%	58.85	7.32	16.17	21.84	0.39	0.43	——
Geese........	7	54.26	7.10	16.21	20.69	0.54	0.43	0.77
Guinea pigs..	6	54.12	7.36	16.78	20.68	0.58	0.48	——
Squirrel......	9	54.09	7.39	16.09	21.44	0.40	0.59	——

As will be seen from the table, there are extraordinary resemblances existing between the oxyhæmoglobin of different animals, which are further shown in the spectroscopic relations as well as in the power of entering into a loose combination with the oxygen of the air, and yielding it up again in a vacuum. On the other hand there are differences in the amount of iron, sulphur, and phosphorus contained in each, the varying solubility and the different forms of the crystals, which prove that there is not a complete identity.

From the above analysis Preyer has determined the formula for hæmoglobin $C_{600}H_{960}N_{154}FeS_3O_{179}$. It is not surprising that the constitution of this large molecule is not yet known. It is highly probable, however, that in this molecule are combined several albuminoid bodies with pigments (hæmochromogen and hæmatin) containing iron. For when hæmoglobin, which is not a very constant compound; is decomposed we have albuminoids, volatile fatty acids, and the already mentioned pigments containing iron.

In what form the iron is combined with the hæmoglobin molecule is not known with certainty. It can, however, be considered as entering into organic combination, for the blood gives no iron reaction. According to Hoppe-Seyler, the old dispute as to whether iron is present in hæmoglobin as a metal or oxide is without foundation, the question now being only whether it exists as a ferric or ferrous compound. When hæmatin is decomposed the iron appears as a ferrous compound (sub-oxide), but that does not prove that it exists as such in the hæmatin. Since hæmatin, when subjected to the different conditions under which the oxide of iron can be changed to sub-oxide, immediately gives up its iron, the atomic structure being otherwise but slightly changed, it is very likely that the iron is present as a ferric compound in such combination that it is easily detached from the molecule. When we study the relationship existing between the iron atom of the

hæmoglobin or hæmatin to the oxygen existing in loose combination in the coloring matter of the blood we find that for every atom which it contains oxyhæmoglobin can absorb 2 atoms or 1 molecule of oxygen under ordinary atmospheric pressure (Hoppe-Seyler.)

These remarks hold good only for oxyhæmoglobin which is saturated with oxygen. In the living blood, however, which gives off large amounts of oxygen in the capillary system and absorbs oxygen in the pulmonary circulation, the degree of oxidation of these iron compounds is constantly varying, being higher in the arterial blood and lower in the venous.

The exceeding probability that the oxygen of the blood exists in combination with the iron of the hæmoglobin, is shown by the fact that the degree of saturation of the blood with oxygen is exactly proportionate to the amount of iron and hæmoglobin contained in the blood, (Quinquaud's method of determining the amount of hæmoglobin depends upon this fact); and furthermore, that as the percentage of hæmoglobin and iron rises and falls, the amount of oxygen absorbed is increased and diminished.* The fact that the same reagents which reduce the sub-oxide and oxide of iron and their salts, have a similar action upon the blood is in favor of this view, as is the further fact that solutions of sub-oxides rapidly attract oxygen from ordinary air and change into solutions of oxides. Finally, the amount of oxygen that could combine with the iron in a given quantity of blood is just about what quantitative analysis shows the actual amount of oxygen to be.

1 grm. of hæmoglobin contains 0.0042 grms. of iron. Now if 1 part of iron in hæmoglobin can combine with 2 parts of oxygen, then every grm. of hæmoglobin containing 0.0042 of iron combines with 0.0024 grms. of oxygen. But according to Hoppe-Seyler, Preyer, and others, 1 grm. of hæmoglobin contains 1.25cc. of oxygen, measured at 0° and 1m. of pressure, that is to say, 0.00235 grms. oxygen.

Variations in the percentage of hæmoglobin and iron contained in the blood.—The percentage of hæmoglobin together with the percentage of iron and the amount of oxygen present in the blood are very variable, even in the same individual, and more so in different individuals (*a*) when the blood has passed through organs in which it has given up water or in which new blood globules have been formed, as for example kidneys

* Compare article on oxygen.

and spleen, it is richer in solid constituents and iron. It contains less of these, however, after it has passed through organs in which it takes up water, or in which the blood globules are destroyed (venous blood from the liver.)

(*b*) That the blood is more or less concentrated according to the amount of water absorbed needs no proof. The effect of food, however, upon this point is not so clear. The following are the results of investigations. A diet poor in albumen and nitrogen, and a large deposit of adipose tissue in the body diminishes the amount of iron and hæmoglobin (Subbotin, Panum.) For this reason the blood of the herbivora is poorer in iron than that of the carnivora. In a dog after eighteen days of pure animal diet, 12.75% of iron were found in the blood ash, while after twenty days of a bread diet only 8.65% were found.

Foster found that in the animals which he fed upon a diet deprived of salt, the amount of iron excreted was never interrupted, and that always a larger amount was excreted than was taken in. During thirty-six days, 0.93 grms. of iron were taken in with the diet, and 3.59 grms. were excreted, so that the body lost the enormous amount of 2.66 grms. of iron. Vierordt found upon himself, by examination made by means of his fine method of spectroscopic analysis, variations between the relative quantities of hæmoglobin from 1.125–1.393. Dietl also found that under an insufficient supply of iron, 1.863 grms. of iron more per day were excreted than were absorbed.

(*c*) Although we have not tables indicating the relative amount of iron in various individuals and different species of animals, yet we have tables of the number of blood corpuscles, and, with the increase and decrease of these, the percentage of iron varies. From these we arrive first at the conclusion that the stronger animals have the largest and the weaker the least amount of iron and blood corpuscles. Andral and Gavarret and Delafond found on an average $93\frac{0}{00}$ blood corpuscles in the blood of the sheep. The strongest cheep had $101–123\frac{0}{00}$. The blood of dogs had on an average $136–165\frac{0}{00}$ corpuscles. One very powerful dog had $186\frac{0}{00}$.

According to Lecaun—

The blood of strong men has.........	$136\frac{0}{00}$	Blood corpuscles.
" " " weak " "	$116\frac{0}{00}$	" "
" " " strong women	$126\frac{0}{00}$	" "
" " " weak "	$117\frac{0}{00}$	" "

According to Prévost and Dumas, the blood of birds has the

largest amount of blood corpuscles and iron. Then comes that of the carnivora, then herbivora, and finally the cold-blooded animals.

(*d*) By comparative observations of the blood at different ages, we learn that the newly-born pup has a blood richer in solid constituents than that of the mother; as the animal grows, the blood becomes poorer; when growth is completed, it again becomes richer, without, however, attaining the original percentage of solid constituents, which it had immediately after birth. We also learn that the percentage of red corpuscles in the fœtal blood is independent of the blood of the mother; the manufacturing of blood corpuscles, therefore, appears to be one of the functions of fœtal life. Lastly, that more iron is present in the blood of the newly-born than in that of adults. According to Denis, Lecanu, and Stoelzing, the number of blood globules and therefore the amount of iron increases from the 1st to the 40th year, then gradually diminishes.

(*e*). The amount of hæmoglobin and iron contained in the blood of men is greater than in that of women.

	According to Becquerel and Rodier.	Denis.	Nasse.
Average amount of iron in men's blood is	$0.565\,^{0}/_{00}$	$0.63\,^{0}/_{00}$	$0.5824\,^{0}/_{00}$
" " " " " women's " "	$0.511\,^{0}/_{00}$	$0.49\,^{0}/_{00}$	$0,5453\,^{0}/_{00}$

According to C. Schmidt in 1,000 grms. of blood there are—

	Blood Corpuscles.	Hæmatin.	Iron.
In healthy men	513.02 grms.	7.70 grms.	0.512 grms.
" " women	396.24 "	6.99 "	0.489 "

(*f*). *In Disease.*—The older investigations were made mostly on blood obtained by blood-letting, and have, therefore, very little value, for blood thus obtained is already greatly altered, apart from the fact that these observers made no allowances for individual variation nor for those of sex and age. Quincke and Wiskemann, however, have arrived at very important conclusions. The following table gives a statement of the results obtained by the best observers, which we have calculated upon a uniform basis:—

In 1,000 grms. of blood there was of iron—

In six healthy full-blooded men,	0.547 grms.	Becquerel and Rodier.
" one " " " woman,	0.544 "	" " "
" men affected by an inflammatory *disease,*	0.490 "	" " "

In women affected by an inflammatory disease,	0.480 grms.	Becquerel and Rodier.
" pleuritic patients,	0.461 "	" " "
" four men affected by acute rheumatism,	0.452 grms.	" " "
" thirty anæmic individuals,	0.366 "	" " "
" chlorotic patients,	0.319 "	" " "
" " "	0.223 "	H. Quincke.
" Leucæmia,	0.244 "	" "
" Healthy women,	0.603 "	" "

The calculations of Quincke are based upon the amount of hæmoglobin present, and on the supposition that the percentage of iron in hæmoglobin is 0.42 and is always constant. As will be seen from this table, the difference between the percentage of iron contained in the blood of chlorotic and leucæmic patients and that of the normal blood is very great.

(*g*). A loss of blood is followed by a reduction in the amount of blood corpuscles and the amount of iron in the blood ; the percentage of fibrin and the solid constituents of the serum are less affected.

THEORY OF THE ACTION OF IRON.

There is no longer any doubt that iron is absolutely necessary to the formation of hæmoglobin and red blood globules, and without any direct proof to the contrary this follows as a direct consequence of the fact that neither hæmoglobin nor blood corpuscles exist without iron. Kölliker, Erb, Recklinghausen and Neumann have shown that the red blood globules are developed from iron.

BLOOD GLOBULES OF THE MARROW AND SPLEEN.

In chlorotic individuals the white corpuscles are increased in number to an extraordinary degree, while the red ones are more and more diminished. When iron is introduced, however, the white corpuscles rapidly absorb it, and a great increase of the red corpuscles sets in, the white being diminished in quantity. Although we do not know the exact process by which this transformation of white into red blood globules is produced, yet no other supposition is left us than that such a change does occur under the influence of the iron.

Rabuteau observed by the aid of the Malassez' blood corpuscle counting apparatus, the increase of red blood globules which took place in a chlorotic girl to whom 0.05 grm. of iron were administered daily for twenty days.

	Blood Corpuscles.
December 4th, previous to the administration of iron, there were in 1 cmm. of blood	2,919,000
Dec. 7th, during the taking of iron, 1 cmm. of blood contained,	3,486,000
" 12th, " " " " " 1 " " " "	3,696,000
" 24th, " " " " " 1 " " " "	4,578,000

So that there was an average daily increase of 82,950 red blood corpuscles to the cmm. and the girl was discharged, cured, at the end of the given time. Duncan and Stricker, who consider chlorosis due rather to a change in the composition (that is to say diminution in the amount of hæmoglobin, sp. gr., etc.,) of the blood corpuscles than to a diminution in their number, observed in an anæmic boy, that an improvement in the diet and the administration of iron were followed in ten weeks by an increase in the amount of hæmoglobin of almost 25%. Quincke observed in chlorosis that the use of iron and a proper diet caused the proportion of iron and hæmoglobin in the blood to be almost doubled in the course of ten weeks.

In the analogous disease of vegetable life, the chlorosis of vegetables or want of chlorophylle, the green coloring matter of the plants, we have also proof that the trouble is a scarcity of iron, and that when this is supplied to the roots in the shape of iron salts, the trouble is cured. "It may be uncertain that iron enters into the chemical formula of chlorophylle (Verdeil), but this we do know, that when the iron salts are withheld from plants they cease to manufacture chlorophylle, so that this substance (iron) is necessary for the green coloring matter. And since plants which depend upon their own assimilation cannot exhale oxygen without the presence of chlorophylle (without which process the formation of organic substances out of carbonic acid and water cannot be conceived), therefore the iron, upon which the production of chlorophylle depends, is of the highest importance to the assimilative processes (Jul. Sachs.)

Although this fact is no proof that the coloring matter of the blood has a similar relationship to iron, yet in connection with the other facts it at least seems highly probable.

Not only in disease but also in health a further increase in the number of blood corpuscles is brought about by the addition of iron. But the observations are too few to make us certain of this fact, especially since we do not know the normal number of blood corpuscles. The table given above shows that the healthy "full-blooded" men of Becquerel and Rodier *had less iron in their* blood than the "healthy women" of

Quincke, whom he does not term "full blooded." Although we shall leave the question open, we shall still express the opinion that we do not believe in a so-called plethora produced by long continued use of iron (without at the same time additional supply of albumen), at least not in the sense of an excess of red blood globules. For an increase of these beyond the normal would necessitate a more rapid metamorphosis of material in the body, accompanied by a more rapid destruction of red blood corpuscles and increased excretion of nitrogen and iron; they would thus be bringing about their own annihilation. Besides, according to Voit, an improvement in nutrition is accompanied by an improvement in all organs equally and not in the blood alone. The observation that in tuberculosis the use of iron often leads to hæmoptysis cannot be explained by supposing the iron to have produced a condition of plethora ; for a return to the normal blood pressure is sufficient to explain the rupture of the thin walled vessels or those lying free in cavities of the lung. In addition to this we rarely find in the histories of these patients that the hæmoptysis was preceded by an abnormal blood pressure (plethora.)

INFLUENCE OF IRON UPON THE FUNCTIONS OF THE ORGANS.

The use of the iron in the blood is, as we have seen, intimately connected with that of the oxyhæmoglobin, and depends principally upon the fact that both of these take up oxygen from the air in the lungs, hold it in weak combination and yield it up again to the tissues of the body. The amount of oxygen absorbed depends partly upon the amount needed for the tissues, and partly upon the amount of iron and hæmoglobin in the blood. The oxygen absorbed by the blood serum dwindles to almost nothing, when compared with the amount transported by the hæmoglobin. Hæmoglobin and iron being the chief oxygen carriers are therefore concerned in all the processes of oxidation—that is, in the life of all the organs in the body.

Whether the iron as such, in addition to these functions, also has a direct influence upon the animal tissues and whether, like the other metals, (lead, copper and mercury) it produces certain changes in the functions of the different organs is unknown. We only know that iron is found in almost all of the organs (bones, teeth, nerves, muscles, liver, spleen, etc.,) and that it is a special constituent of almost all of the pigments and the hair. It is not positive, however, whether the iron present in these organs is really deposited in the cells of the tissue or

whether it is only present as a constituent of the blood which they contain; this is especially true of the bones, teeth, muscles, and nerves. In the liver and spleen it is highly probable that iron is deposited in the cells of these organs; for Oidtman—Scherer state that the percentage of iron in the liver is very large, (2.7 %) and according to Scherer, the percentage of iron in the spleen is also very large. H. Nasse found miscroscopic granules, which, as far as could be ascertained, consisted of iron oxide; in very old and lean horses, the dried spleen pulp yielded almost 5 % of iron, at least four times as much as in young animals. According to Quincke, the spleen, the parenchyma of the lymphatic glands, as well as the marrow of the bones often contain iron albuminate, which can be demonstrated by the use of ammonium sulphide. That which is present in the cells of the spleen, in the form of granules, probably originates from destroyed red blood corpuscles and is again used for the formation of new ones (physiological siderosis). Pathologically, siderosis has been seen in pernicious anæmia and diabetes mellitus.

For the establishment of the hypothesis of a direct iron action, which is independent of the iron present in the hæmoglobin, only a single observation by Pokrowsky and Botkin can be utilized. These observers report, that even a few hours after the taking of an iron preparation, that is to say, long before it is possible for a noteworthy increase in the number of red blood globules to have set in, a rise in body temperature takes place. They, therefore, considered this as a direct effect of the iron; for thus the finer arterioles could be contracted, and thus increased blood pressure, tissue metamorphosis and temperature result. With this may be connected the rapid improvement in nutrition, and the equally rapid disappearance of œdematous transudation. We need not mention, however, that this view, which was held by Gasse also, is entirely unfounded, as is also the assertion of the latter, that iron can take the place of the red blood globules in the blood!

We can, therefore, only consider iron important as taking part in the formation of the blood corpuscles, and thus as a carrier of oxygen, and as without any effect upon the organs themselves. Its normal function, indeed, lies in the fact, that the health of the body depends upon its presence in normal quantity. We can not ascribe under any conditions a specific effect to the normal absorption of iron or its presence in the blood in normal quantity, further than that *it enables all organs to carry on their normal functions*. We can not believe that it

causes an increase of any of the normal functions, the normal temperature, normal frequency of the pulse, normal tissue metamorphosis, etc. The statements so generally made, that iron continued for too long a time, or iron administered to patients who are already of a "plethoric" disposition, causes flushing, palpitation, a tendency to congestions and even hæmorrhages, seem to be the result of *a priori* reasoning. For nowhere could we find any proof for such a statement, and furthermore, observations made upon those living in the neighborhood of iron springs, who use the iron waters as a daily drink, not only failed to show any plethoric individuals, but on the contrary revealed a wonderful frequency of anæmic conditions. Even the frequently cited observations of Pokrowsky, of an increase in the normal temperature, can not be utilized for the support of this view, since they were made upon sick people. When Pokrowsky here speaks of normal temperature, he means not the temperature of healthy people, but a normal degree of temperature present, however, in sick people, which is not the same thing as a normal temperature in healthy people. In the same manner his assertion that the use of iron is followed by an increase in the excretion of urea can not be applied to healthy people, apart from the fact that Pokrowsky did not determine the daily amount of nitrogen taken into the body, so that the increased excretion of nitrogen may just as well have been due to an increased absorption of this element in the diet as to the iron. Indeed, were the excretion of nitrogen really increased only on account of the iron absorbed thus, there should have been a diminution in the bodily weight. But P. talks even of an increase in the weight of the body.

The great importance of a normal percentage of iron and hæmoglobin in the blood, is best seen when the latter is diminished from some cause, in which case we have the condition known as chlorosis. In chlorotic patients we see every function disturbed, and both mental and bodily activities deeply depressed. Profound mental depression, indisposition to work, enjoyment or motion, muscular weakness, weakness of the beat of the heart, and slow and shallow respiration, loss of appetite, disturbances of digestion and of all the secretions, headache, dizziness, disturbed sleep and sleeplessness. That the lack of iron is really the cause of all these symptoms is shown by the rapid improvement which follows the administration of iron to these patients.

In chlorotic and anæmic subjects, iron causes an increase *of all the functions* (tissue metamorphosis, temperature, heart puls-

ation, blood pressure, etc.,) *but only up to, and not beyond the normal.*

The increase in the amount of hæmoglobin is above all the cause of this rapid return of the functions to their normal standard, but this result is also favored by the increased secretion of gastric juice and the improved digestion resulting therefrom.

For a long time it was unknown how a lack of iron in the blood could occur, since enough is supplied to the organism in the daily food. But it appears probable that chlorosis is generally preceded by a longer or shorter period of insufficient nutrition, which may be the result of a loss of appetite and disturbed digestion.

We have already shown by the observation of Forster and Dietl given above, that with the diminished supply of iron, its excretion still continues, so that the blood loses more iron than it receives.

Injection of salts of the sub-oxide and oxides of iron into the blood do not, as Blake first showed, make the physiological action of iron any clearer, nor indeed do they even explain it. For all of the results of such procedures, the cardiac and vasor symptoms, and finally paralysis of the heart and death, are due to coagulation of the blood, and the lodging of emboli in important organs, and not to the iron as such (Quincke).

THERAPEUTIC APPLICATION.

Iron is one of the very few remedies of whose therapeutic value physicians have always been convinced. And although in recent times, doubts have arisen whether it really accomplishes all that is claimed for it, yet manifold experience has taught us that in certain conditions it is an excellent, and often an indispensable remedy. We shall consider the peculiar effects of individual preparations in certain conditions, when we come to consider these preparations themselves. Here we shall only give the indications for iron as such, referring only to those preparations which produce a purely iron action without any particular accessory effect.

Even long before the extreme physiological importance of the iron for the blood, and indeed for the whole organism was known, experience had taught that by its use conditions of disease, which were caused or accompanied by a general deterioration of the blood or a diminution in the number of red blood globules (*oligocythæmia*), were cured, or the patients materially

aided, at least, in their restoration. These conditions are those termed the "anæmic" and "cachectic." We need not again consider the *modus operandi* of the iron action in those conditions, since this was thoroughly discussed under the head of physiological action, to which we here refer. We shall here, therefore, only consider the clinical features.

The utility of the iron in the various forms of anæmia is as follows:

Iron is a most valuable remedy in the treatment of chlorosis, a condition particularly common in females at the period of their most active development (to the so-called false chlorosis we shall soon refer). This condition, with its various symptoms, is improved by the continued use of iron preparations and rapidly dissipated. It is only in old and very severe cases that a complete cure is not effected, only temporary relief from the symptoms following, all of which return when the drug is suspended. With the iron should be combined other means for improving the strength of the patient, such as a nutritious milk and meat diet, exercise in the open air, etc. In recent times the greater portion of the good effect has been ascribed to these improved dietetic and hygienic conditions; but although these are very important and indispensable, yet experience teaches, that iron not only hastens the curative effect, but that it is indispensable for the cure of complete forms of the disease.

A consideration of the condition of the digestive apparatus, especially of its digestive power, is of great importance to the treatment. When there is a real gastric catarrh present, it must be removed by proper treatment before the course of iron is begun; but when the dyspepsia is the direct result of the chlorotic condition, it is best and most quickly removed by the use of iron. Since, however, it is not always easy to distinguish between digestive disturbances as such, and those which are the result of anæmia, it is best to begin the treatment by small doses of an iron preparation which is readily digested. In chronic constipation, iron can be very well administered, but it should be combined with extractum rhei. We must here also mention that some individuals have a peculiar idiosyncrasy against certain iron preparations. In these cases we must try until we reach the proper preparation. Finally, we must state that daily experience teaches that a satisfactory result is only attained after long continued use. The rule that a chronic disease requires chronic treatment is certainly here applicable. It is often necessary to intermit the use of the remedy, even

where constant improvement is taking place, and then, after a time, recommence the treatment.

The use of large doses as recommended by the great clinicians, such as Trousseau, is entirely unnecessary.

Apart from chlorosis in the narrower sense of the word, iron can be used with good result in various anæmic conditions, such as the conditions of malnutrition, which are the sequellæ of acute diseases that have lasted a long time, as after typhus, puerperal fever, pleurisy, etc. In these cases, however, iron has not the same value as in chlorosis; for complete recovery results here even when only dietetic regulations have been prescribed. It is more necessary for individuals who have been greatly weakened through great loss of blood, provided it was not through hæmoptysis or the so-called active hæmorrhages. For in these cases iron is directly injurious. The "iron cure" (especially iron baths, connected with dietetic regulations) has shown itself of value in cachectic conditions due to venereal excesses, or long continued pollutions, or the result of chronic diarrhœa or chronic bronchorrhœa, provided that in the latter cases there be no fever or inflammation going on.

Among these conditions we should mention morbus Basedowii. Although we cannot explain its action in this disease, yet experience has shown, that by the so-called tonic treatment, in which iron takes the chief part, an excellent result is obtained, especially if the individual be anæmic and pale. Of course, the iron is contra-indicated if (as sometimes happens) the patient suffering from morbus Basedowii, be strong and look rather cyanotic than pale. We lay the more stress upon this point because sometimes iron is ordered indiscriminately for every case of Basedow's disease.

The malarial cachexia, which is the result of severe and long continued intermittent fever, is more rapidly cured, when, in addition to the change of location and quinine, we order iron preparations. The iron preparations hold a chief place in the treatment of the so-called *anæmic dropsy*, due to a hydræmic condition of the blood, and in which disease of the lungs or heart has been excluded. So also in the cachectic hydrops, following after intermittents, severe acute diseases, long continued suppuration, etc. The hydræmic condition of the blood, which is present in chronic nephritis, and accompanies the dropsy dependent upon this trouble, has often been treated by iron preparations without any very noteworthy beneficial result. Finally iron is frequently used in the dropsy due to amyloid degeneration *of the kidney*. In these cases, and indeed in amyloid de-

generation of any other organ, it is generally given in combination with iodine. Even if the process, after it has made some progress, is not cured, yet this treatment, combined with general measures, serves to retard the progress of the malady.

In scrofula and rickets, accompanied by decided anæmia, the iron, in combination with other fitting remedies (iodine, etc.), does good service. Opinions differ, however, as to its utility in syphilis. For while some praise its effectiveness in the cachexia which is the result of the syphilitic process itself, or of the remedies which have been used for its cure, others are opposed to it in this affection (as, for instance, Bærensprung); according to these latter observers, it causes the symptoms of latent syphilis to reappear. In the carcinomatous cachexia, the iron preparations may be administered, but it would be folly to expect, as was formerly held, that this drug has any influence upon the cancerous process itself.

The use of iron in phthisis deserves a special notice. Morton taught, that sometimes it aided in prolonging the life of these patients, but he used it only on condition that no trace of fever or any tendency to hæmorrhage was present. The experience of the most reliable observers tends abundantly to show that it is wisest to banish iron entirely from the therapy of phthisis. Louis and others advise entirely against its use. We shall speak of this point again later on.

In addition to the large class of anæmic affections which we have just discussed, iron preparations have been used in various other conditions. Apart from those uses for which the necessary effect is not present, to an equal degree in all of the preparations of iron, such as the astringent, hæmostatic effect, etc., which we shall consider in the proper place, iron compounds have been used for the anomalies of menstruation. In menstruatio erimia it can, of course, only be used as a direct styptic. In amenorrhœa, however, it is useful, but only when this condition is the result of anæmia. In many affections of the nervous system, chalybeates and especially the carbonate of iron have been used. The iron has not a so-called "specific" action in these neuroses. The good effect which has been observed, appears to occur only when a certain degree of anæmia exists as the cause of the neurotic condition. So that iron would be of great utility in the neuralgias of chlorotic patients.

We have already mentioned some of the conditions in *which the iron preparation must either not be used at all or used with great care.* They should never be used in febrile affections. An augmented frequency of the pulse, prohibits them only

when it is a symptom of a febrile condition ; if, however, it be a symptom of an anæmic condition, the use of iron is, on the contrary, indicated. Furthermore the use of iron must be avoided in the so-called plethoric individuals in whom there is decided tendency to cerebral congestion, a condition known as the "apoplectic" habit. Of course we do not mean that a single styptic dose of, for instance. liq. ferri, can not be given when needed ; but it is the continued use of iron in these patients that we advise against. In individuals with a transparent skin and with the so-called tuberculous habit, in whom the tendency to hæmorrhages is shown by frequent epistaxis iron should not be used. Yet in these very cases the mistake is often made of ordering iron to counteract an imaginary anæmia, with the result usually of causing a hæmoptysis. These are the cases known as "false chlorosis." When this condition is present in young men mistakes are easily avoided ; but with greater difficulty in young girls. The presence of a beginning infiltration of the apices of the lungs will produce symptoms simulating chlorosis, while the true condition will not even be evidenced by a cough. If in these cases or in the tuberculous diathesis, a very careful physical examination is not made, or if the iron be not rather excluded in doubtful cases, we may often see that while under the use of the iron the appetite and strength certainly increase, and the cheeks grow redder, yet hæmoptysis and phthisis set in. There are, however, a number of observers who do not consider commencing phthisis as a contra-indication for the use of iron, but order it even when symptoms of infiltration have already set in. The few cases of this sort in which we have given iron, do not encourage us (hæmoptysis having rapidly set in) to adopt the views of the latter observers. We will acknowledge, however, that concerning this point detailed statistics are wanting, and that it is possible that iron does good in certain of these cases ; at present, however, we should advise against its use. Chalybeates are contra-indicated in organic valvular diseases of the heart, especially those in which the patient has a cyanotic look, and the pulmonary circulation is retarded, that is to say in insufficiency of the mitral valve, or stenosis of the ostium venosum sinistrum. Their careful use, however, is allowable, when, with the heart trouble there is paleness, that is to say in insufficiency of the aortic valves ; also in recent disease of the valves, of whatever kind, when compensation has not yet set in, when the patient is just recovering from severe articular rheumatism, and when the patient is debilitated and pale. That the

use of iron presupposes a normal condition of the digestive tract and digestive functions, and that it should only be used in the digestive disturbances which are the result of anæmia, we have already mentioned. Finally, we should mention that when menstruation regularly sets in profusely, the iron should be suspended a few days before its appearance.

As to the methods of the administration of iron, experience has long shown that the large doses formerly used not only do not produce a quicker and better result, since after all only small quantities of the drug can be absorbed, but that such doses really do harm, by disturbing digestion by mechanical irritation. The administration of 0.1 to 0.2 grms. 2 or 3 times daily is fully sufficient to produce the iron effect. The best time for its administration is when the gastric juice (which as we have shown is of importance to the absorption of the iron) is being secreted in largest amounts, that is to say during stomach digestion.

Externally iron is very much used, to produce a local effect, as an astringent, etc. This will be discussed under the individual preparations. Iron baths are very much used to produce a general iron effect. We have already stated, however, that absorption through the skin does not take place. The benefits obtained from the use of "iron baths" are probably derived from the bath as such, or from the substances derived from the bath, such as carbonic acid, etc. The iron certainly has nothing to do with it; a very small amount of iron may be thus absorbed by the mucous membranes of the genitals in women.

The various iron preparations.—The number of these used in medicine is very large and no particular difference between them can be given as an excuse for such lavishness. We shall therefore only specify the most important of them, discussing with greater completeness only the chief representatives of the various groups which show some essential difference in their action.

The differences, however, as we shall soon show, exist only between concentrated doses of different preparations. In very small or very dilute doses all have, without exception, the general iron effect, which was considered in the introduction.

For therapeutic purposes we really need but few preparations.

PREPARATIONS EXERTING A PURELY IRON ACTION.

Each of these in small doses exerts a purely ferruginous action; it is of little importance whether the sub-oxide or the oxide be used. It is generally

administered in combination with aromatic drugs, such as cinnamon, orange peel, etc., in order to stimulate the excretion of the gastric juice, and thus perhaps to prevent or diminish the digestive disturbances which iron is apt to produce. To this class belong the following preparations.

1. *Ferrum pulveratum—Iron powder.* A fine, heavy, ash-colored powder, which dissolves in the gastric juice, hydrogen and sulphuretted hydrogen (it being often combined with iron sulphide) being librated. From 0.1–0.5 per dose (2.0 pro die) in powder or pill.

2. *Ferrum hodrogenio reductum.*—Iron reduced by hydrogen. This is a finer powder than the previous preparation, and is free from iron sulphide. It is a tasteless predaration, and being thus distinguished from the others, is the more agreeable of application; from 0.05–0.25 pro dosi (1.0 pro die) in powder, pill or pastilles.

3. Ferrum oxydatum fuscum s. hydratum, ferric oxide hydrate, Fe_2O_3 $3H_2O$, is a fine reddish brown powder, insoluble in water, odorless and tasteless—from 0.1–0.5 pro dosi (2.0 pro die) in powder or pill.

4. Ferrum oxydatum saccharatum solubile, iron sugar, is a brownish-red powder of a sweetish, inky taste, of doubtful composition and easily soluble in water. Since it contains only 3 % of iron it must be given in large doses (0.5–2.0 grms.)

5. Syrupus ferri oxydati solubilis—iron syrup—is a clear brown fluid of a sweetish puckery taste, administered in teaspoonful doses, since it contains only 1 % of iron; up to 30.0 grms. pro die.

*6. Ferrum carbonicum oxydulatum—iron carbonate.—Co_3Fe—is very easily decomposed and changed into the ferric oxide hydrate. This is the form under which iron is present in many iron springs. Has no advantages, however, over the other preparations.

Therapeutically peculiar effects have been ascribed to this preparation. The affections in which it has been most recommended are neuralgias and chorea. Among the first it was particularly recommended for neuralgia of the fifth (Hutchinson and many others.) Positive results obtained from its use, however, are opposed by many negative ones (J. Franck and others). So that, although the utility of the ferrum carbonicum is not to be doubted in the face of so many direct assertions, it still remains questionable when it should be used with an expectation of good results. According to all experience this preparation does no more than is accomplished by iron in general in neuralgias; that is to say, it relieves those cases in which anæmia is either the cause or accompaniment of the neuralgic condition. The large doses, therefore, in which it has been given are entirely superfluous (1.0–5.0). We must not overlook the fact, that in some of the many cases that have been recorded as having been cured by this remedy, it is particularly stated that the constitution was strong, and neither chlorosis, nor any cachectic conditions were present. The same may be said of the use of the iron carbonate in chorea and other neuroses.

The preparation is given in from 0.05–0.5 grms. doses—in pills (with rad. althaeae) once a day.

7. Ferrum carbonicum saccharatum—a grayish green powder, with a sweetish puckery taste, containing 20 % of the ferric carbonate, which keeps better than the preceding preparation. Also contains sodium bicarbonate and sugar. From 0.5–2.0 grms. pro dosi (10.0 pro die); in children 0.03–0.1 three times a day.

Pilulæ ferri carbonici s. ferratæ Valleti; every pill contains 0.05 of ferri carbon.

8. *Ferrum chloratum*—iron chloride.—FeCl—is a pale green, hygroscopic

and easy soluble salt, which rapidly oxidizes in the air. It certainly does not deserve the praises whieh Rabuteau gave it, if only for the reason that it is easily converted into iron chloride in the air,

From 0.01–0.1 pro dosi (0.5 pro die).

9. Ferrum lacticum—lactate of the sub-oxide of iron—a yellowish powder with difficulty soluble in water. It is not, as was believed, more easily assimilated than the other preparations. From 0.05–0.3 pro dosi (1.0 pro die) in pills, powder and pastilles.

Other preparations, such as ferrum citricum oxidatum, ferrum citricum ammoniatum, ferrum phosphoricum oxidulatum, ferrum pyrophosphoricum cum ammonio citrico, sodium pyrophosphoricum ferratum, extractum ferri pomati (see tinctura ferri pomati) are all superfluous. Dose of all of them about 0.1–0.5 (pro dosi) 2.0 pro die. Ferrum pyrophosphoricum—the French preparation in which the ferric pyrophosphate is given (in combination with other salts, since by itself it is almost insoluble in water) is not used by us. But we do use at present a water containing the pyrophosphate of iron, which contains about 0.05 grms. of the drug dissolved in 150 grms. of fluid. It is therefore a favorite form of mineral water to prescribe for anæmic subjects, in whom the digestion is very easily disturbed.

Iron waters.—The extraordinarily large use or rather misuse of the iron drinking and bathing waters, which was common in the early portion of the present century, has given place at the present time to a more moderate use of these waters. For iron baths, however, we can give no indications, since iron is entirely ineffective when taken in the form of a bath (compare page 180).

The indications for the use of the iron drinking waters are the same as those formulated for the use of iron in general ; we therefore refer to these simply. There are several circumstances connected with the use of natural iron waters as compared with pharmaceutical preparations, which must be considered. They are these,—that foremost of the cases in which the iron preparations are indicated, the circumstances under which the mineral waters (iron) are taken, materially assist the therapeutic action of the iron itself ; these are exercise, fresh air, sometimes even mountain air, increased appetite, etc. In addition to the variations in climate, elevation above the sea, etc., which the various iron springs offer, we must also consider the presence of any active ingredients in the water in addition to the iron, such as sodium chloride, glauber salts, sodium carbonate, etc. It is by a consideration of all of these that we shall be enabled to select the proper spring for individual cases.

Iron is present in most springs as the ferrous bicarbonate, in a few as the ferrous sulphate. The former occurs in quantities varying from a mere trace to considerable amounts, in some of the alkaline, alkali-saline, and sodium chloride waters, without these being prescribed as iron springs. For this purpose only those are used, the waters of which contain almost exclusively iron, or when, at least, this metal forms a considerable percentage of the solid constituents. Even the strongest of these waters, however, contain but little iron, most of them contain on an average 0.1 grms. of iron carbonate to 1 kilo. of water. All of the iron waters are cold, the warmest having a temperature not higher than 20° C. The locality of the spring, as regards climate, and especially elevation above the sea level, is of great importance to its general effect. The most elevated is St. Moritz (about 5500 feet). Then there is a whole series between 2000 and 1000 feet : (Reinerz, *Rippoldsau, Antogast*, Griesbach, Elster, Alexisbad, Lobenstein, Franzens-

bad, Altwasser, Cudowa, Petersthal Liebenstein, Spaa, etc.; below 1000 feet we have Schwalbach, Bruckenau, Driburg, Boklet, etc).

The most important springs are the following :—

a. Pure iron springs, or at least those that have a pure iron effect, the other constituents not altering this—1. Schwalbach, in Taunus ; 2. Spaa, in Belgium ; 3. Alixisbad, in Harz ; 4. Altwasser and Flinsberg, in Silesia ; 5. Bruekenau, in the Rhone hills (very weak) ; 6. Freienwalde, Province of Brandenberg, near Berlin ; 7. Lobenstein, in the Principality of Reuss ; 8. Liebenstein, in Meiningen ; 9. Muskau, in Oberlausitz, containing considerable quantities of the ferrous carbonate and sulphate, with only traces of carbonic acid ; little used.

b. Alkali saline waters containing iron—Franzensbad Elster, Marienbad and Tarasp.

c. Sodium chloride waters containing iron—Kissingen, Kreuznach, Rehme and Duerkheim.

d. Iron springs with considerable quantities of Glauber salt, magnesia and lime carbonates and magnesia and lime sulphates. 1. Pyrmont, in Waldeck ; formerly considered the type of iron waters, and frequently visited. 2. Driburg, in Westphalia ; 3. Boklet, near Kissingen ; 4. Reinerz and Cudowa, in Silesia ; 5. Antogast, Petersthal, Griesbach, Freiersbach and Rippoldsau in Kinzig and Renchthal in Schwazwald ; 6. St. Moritz, in Upper Engadin.

II.—IRON TINCTURES.

In iron tinctures the iron is dissolved in alcohol, ether or wine, so that we have first the effect of these materials (augmented secretion of the gastric juice), and then that of the iron. Here then the alcohol, etc., serve the same purpose as the addition of aromatics to the first group. They are also said to have an exciting effect, although this is not so, for they are never taken in sufficient doses to produce any of the exciting effects of the alcohol and ether upon the nervous system. Therapeutically they are used for the same purpose as the pure iron preparations, and are generally given to weak, delicate individuals in whom the digestive power is at a low stand-point, and by whom they are generally well borne.

1. Tinctura ferri pomati, the mallate of the tincture of iron, consisting of 1 part of extract. ferri pomati and 9 parts of aq. cinamomi spirituosi. The extractum ferri pomati is a very inconstant preparation, which contains on an average 0.7 per cent. of iron. The tincture can only contain 0.7 per cent. of it, and is therefore weak and can scarcely be used for the production of an iron effect ; from 0.5–2.5 pro dosi (10–50 drops).

Tinctura ferri acetici aetherea, consists of 9 parts of ferrum aceticum solutum, 2 parts of spiritus vini rectificatissimus, 1 part of aether-aceticus and contains 6 per cent. of iron. A dark brown fluid, having an odor like that of ether. From 0.5–2.5 (10–50 drops).

3. Tinctura ferri chlorati aetherea—is prepared by mixing 1 part of ferrum sesquichloratum with 14 parts of spiritus æthereus, and presents a solution consisting chiefly of iron chloride, which contains only 1 per cent. of iron ; from 0.5–1.5 (10–30 drops).

To these can be added the tinctura ferri chlorati, the *tinctura sesquichlorati and *tartarici.

Vinum Ferratum, iron wine formed by the addition of iron to Rhine wine, and to be taken by the wineglassful, is one of the many old fashioned

methods of giving iron, although there seems to be no reason why the noble flavor of the wine should be destroyed by the addition of iron, instead of taking the tincture of iron first and following it by the wine.

III.—HÆMOSTATIC IRON PREPARATIONS.

Although when given in dilution these are like the other iron preparations in their effects, yet they are distinguished from the latter by their caustic and strongly coagulative action when used in concentrated form. Their chief representative is the ferrum sesquichloratum or crystallized iron chloride $FeCl_3+12H_2O$ (this must be carefully distinguished from the iron chloride which contains no water Fe_2Cl_3 or Fe_2Cl_6) ; it is a crystalline, yellow, easily soluble mass, having a slight odor of muriatic acid and slowly deliquescing in the air. This salt is used for preparing the therapeutically applied.

1. Ferrum sesquichloratum solutum s. liquor ferri sesquichlorati. Fluid iron chloride. It is a clear fluid, having a yellowish-brown color and containing 15 per cent. of iron or 43.5 per cent. of iron chloride which is free from water.

Physiological Action.—In strong almost tasteless dilution the iron sesquichloride, certainly like all other iron remedies, aids in the formation of blood, being converted into the iron chloride in the stomach.

In stronger dilution it has a very strong puckery taste without exerting any contractile effect upon the bloodvessels in even 10 per cent. solution. This effect is only produced by a 50 per cent. solution, and even then is not as great as that produced by silver nitrate and lead solutions. This contraction affects only the arteries and veins (while the capillaries are dilated) and at the same time the blood contained in these vessels is coagulated, and loses its red color. Solutions that do not produce coagulation do not alter the lumen of the vessels (observations of Rosenstein and Rossbach upon the mesentery of the frog). Its hæmostatic effect is therefore not due to a contraction of the vessels but to coagulation of the blood. But in this coagulating effect it is far superior to any other styptic. One drop is sufficient to coagulate a whole reagent glass full of blood, so that not a drop will fall out when the glass is overturned. This coagulating effect of concentrated solutions, when applied to the living tissues is felt very deep in the tissue. Husemann relates a case in which a traumatic injury of the upper lip and the alveolar process of the superior maxilla was painted with this substance, and sudden death resulted the following night, due to embolism of the brain.

The coagulation of the blood depends in part upon the formation of insoluble albuminates, and in this way also we can account for the caustic effect produced by concentrated solutions upon the skin and mucous membranes. When such a solution is internally administered, gastro-enteritis results and in some cases death.

It was believed that even dilute solutions administered by the stomach could when absorbed into the blood produce a distant hæmostatic effect, as in hæmorrhages from the kidneys, uterus, etc., by contracting the injured bloodvessels, but that this belief is fallacious is shown by the fact that liquor sesquichlorati as such can not circulate in the blood without producing coagulation, thrombi and emboli, furthermore these *dilute* solutions are not hæmostatic even when locally applied.

Therapeutic Application.—This preparation is exclusively used as a styptic. It is, as we have already said, one of the best local hæmostatics and is therefore applied when the hæmorrhage is amenable to local treatment. It is of value in menorrhagia, traumatic hæmorrhages, epistaxis, etc., indeed, when-

ever it can be applied directly to the bleeding point. In these cases it seems to have a more energetic effect than cold; there is danger, however, of embolism resulting from its use. In recent times it has been used for injecting aneurismal sacs, dilated veins and vascular tumors such as angiomata in order to bring about their disappearance. This has sometimes been accomplished, but the dangers of the procedure have very much interfered with its application. These dangers consist in first, that if the iron chloride should gain access to the blood, coagulation would immediately take place, death resulting in a few minutes. This danger can be to some extent avoided by compressing the artery above and below the aneurism, and this should always be done, even in venous and capillary tumors. Again, the irritation of the iron chloride often brings on inflammation from which even death may result. For these reasons iron chloride is to-day but little used for the treatment of these conditions, and other procedures are therefore preferred.

The caustic effect of the remedy is exerted even when locally applied as a hæmostatic, and this may give rise to very disagreeable inflammations.

It is very doubtful whether the iron chloride has any effect upon hæmorrhages from the stomach and intestines, in which it was formerly held as the best remedy. When we observe how accurately the styptic must be applied in superficial hæmorrhages from the skin, to have any effect, it becomes extremely improbable that 5 or 8 drops of the remedy administered in water gruel will come in contact with the small bleeding point when it is brought into the large cavity of the stomach often filled with blood, and presenting such a large surface of mucous membrane. Even more unlikely does it seem that 5 drops will have any effect upon the bleeding of a typhus ulcer. Consider the extent of surface from the mouth to the bleeding ulcer of the lower ileum or cæcum! How improbable that the drug will even reach the bleeding spot in an active form! We as well, as other observers, have convinced ourselves of the fact that severe hæmorrhages from the stomach and intestines will cease without the application of any remedy. The belief that the internal administration of this remedy will have any effect upon hæmorrhages of the lung is entirely unfounded.

Iron chloride takes an important part in the *inhalation treatment.* Although it is very much used by those who believe in the arbitrary application of remedies, yet rational therapeutics limits the use of these energetic remedies for inhalation, only for certain cases, such as profuse hæmoptysis, which cannot otherwise be stopped (Waldenburg). For these substances have many injurious effects, such as local action upon the mouth, digestive disturbances, etc. That it does harm in these cases by inciting to severe cough, has been disproved by experience. The preparation is not suited for inhalation in chronic conditions.

As a styptic we use 5.0–25.0 to 500.0; for inhaling, as an astringent, we use 1.0–10.0 to 500. In other cases in which it is used, as, for instance in blennorrhœa, as an astringent, and in badly suppurating wounds as a dressing, it can be replaced by better remedies.

Dosage—internally, 3–8 drops pro dosi, in some mucilaginous vehicle, such as water-gruel, boiled rice, etc. Externally it is best applied by placing upon the bleeding point wads of cotton or charpie, which have been thoroughly soaked in the iron chloride solution and again squeezed. To very small bleeding points such as leech bites, a few drops can be directly applied. For injection into vascular tumors and dilatations (by means of Pravaz's syringe) we require but a few drops (2–4). As an injecting solution for blennorrhœa, 1.0–5.0 to 150.0–200.0

2. *Ferrum Sulphuratum Purum.*—Pure ferrous sulphate (iron vitriol)

So_4Fe+7H_2O. Light bluish-green crystals, deliquescent and easily soluble. In a damp state and in solution it absorbs oxygen from the air, and becoming brown in color changes into an oxide.

Physologicial Action.—Dilute solutions administered for a long time produce the general effect of iron compounds, but in doing so it disturbs digestion and causes constipation, and these to a greater extent than the pure iron compounds.

In concentrated solution it has a caustic effect on account of its coagulating power upon albumen; internally it is a styptic and produces gastro-enteritis in the same manner, only to a less degree than the sesquichloride of iron, to which we therefore refer.

Its disinfectant and antiseptic power is, when compared with that of other substances, too slight to be worthy of any further notice.

Therapeutic Application.—The therapeutic value of this drug, whether used internally or externally, is such that we can easily do without it. Even the much spoken of disinfecting properties of this salt are very doubtful, and in any case can be replaced by more active substances.

In anæmic conditions iron vitriol is not used, because its continued use gives rise to digestive disturbances. In diabetes, tuberculosis, helminthiasis and intermittents, in all of which conditions it has been recommended, it has not shown itself of much service, and partly even has proved itself directly injurious. If used at all, it may be used as an astringent remedy in chronic catarrhs of the intestinal canal, and even here it can be replaced by better remedies. As a styptic it is also unnecessary. Externally the ferrous sulphate is used in the same conditions in which tannin is used, although the latter drug is used more frequently. To avoid repetition we refer to what is said under this remedy. It has also been here recommended for inhalation, but for this purpose, as a rule, tannin and alum should be preferred, and if a strongly astringent preparation be desired, then we select iron chloride.

For some time iron vitriol was one of the most commonly used disinfectants. In this connection we know positively that it acts as a deodorizer, and being very cheap, its value for this purpose is enhanced, because it is within the reach of all. It destroys the sulphuretted hydrogen smell of fæcal matters and other foul-smelling substances, by decomposing it and combining with the sulphur. The employment of the iron vitriol for this so-called disinfection, or rather deodorization, is, as we have already said, the more practical because of its cheapness. Another question is whether substances which are the carriers and spreaders of certain diseases, are destroyed by the use of ferrous sulphate. For the cholera germ, and in respect to this disease, this question has been much discussed during the past year, it does not appear well established, for sewers which have been energetically deodorized by the use of ferrous sulphate have yet served as the center for the spread of cholera. According to these observations the iron vitriol does not occupy as high a place as a disinfectant as was supposed, and it is certainly inferior in this respect to the mineral acids, phenol and salicylic acid.

Dosage and Preparations.—1. Ferrum sulphuricum purum, internally from 0.01 to 0.1 pro dosi (0.5 pro die) in pill or solution; externally, for bathing, 100–150 grms. for each bath; as an injection for chronic catarrhs, 0.1–0.2 to 10.0; as a styptic, 2.0 to 10.0; as a powder for sprinkling (as a disinfectant, etc.,) generally with carbon, myrrhe, etc., 1 to 2–3.

2. Ferrum sulphurium crudum, only used externally.

3. *F. s. siccum,* in doses half as large as "purum."

4. *Pilulæ alœticæ* ferratæ s. Italicæ nigræ, consisting of equal parts of

ferrum sulphuricum purum and aloe pulverata, blackish in color. Every pill weighs 0.1, 1–2 pro dosi. This preparation is superfluous.

5. Ferrum sulphuricum oxydatum ammoniatum, the ammonio sulphate of iron. Ammoniacal iron alum is said to have an anthelmintic action. An unnecessary preparation.

6. Liquor ferri sulphurici oxidati; fluid iron sulphate; is only used for preparing the antidote for arsenic.

3. *Ferrum Aceticum Solutum—Liquor Ferri Acetici.*—The solution of the acetate of iron, reddish brown, having the smell of vinegar and containing 8 per cent. of iron. Physiologically it acts like the ferrum sulphuricum. Therapeutically it is entirely superfluous.

IV.—IRON PREPARATIONS USED AS ANTIDOTES.

1. Antidotum arsenici, ferrum hydricum in aqua; a solution of the hydrated oxide of iron. Since this preparation decomposes on keeping and thus loses its power, it must be freshly prepared every time before using.

Take 60 parts of the solution of ferric sulphate and 120 parts of water, add to the mixture 7 parts of dried magnesia which have been previously well mixed with 120 parts of water; shake both fluids together until a homogeneous mixture results; the latter is of a reddish brown color, and bitter taste, and consists of a quantity of the hydrated oxide of iron, magnesia sulphate and magnesia usta.

This mixture, first recommended by Bunsen, is one of the best antidotes to arsenic as long as this still remains in the gastro-intestinal canal. When introduced in excess it forms with the arsenious acid, arsenite of iron and arsenite of magnesia. Since these new combinations are insoluble in water, though not in the juice of the intestine, we must not depend entirely upon the administration of the antidote, since absorption of the arsenic may still take place. We should therefore follow the giving of the antidote by an emetic or the stomach-pump, or a strong cathartic consisting of Epsom or Glauber salts may be given, and thus get rid of the new combinations from below.

If the arsenious acid has been already been absorbed into the blood, there is no antidote.

The antidote must be given in great excess. Every 5 minutes 1–3 tablespoonfuls, and this must be continued for some time. It need not be warmed. The dose of Epsom salts afterwards administered should be about 15.0 grms.

*2. Ferro-Kalium cyanatum flavum, potassium ferrocyanide, $K_4FeC_6N_6+3 H_2O$ presents large yellow, permanent crystals, having a sweetish bitter taste.

This salt has not the effect of an iron salt upon the organism, since it does not give up its iron to the blood, but is excreted in the urine as the ferro or ferridcyanide of potash. The only well-observed physiological effect is upon the intestine, an increased peristalsis and as a result it acts as a cathartic.

It is a good antidote against poisoning by the salts of many heavy metals, because it forms with these an amorphous precipitate of an insoluble ferrocyanide.

It is especially recommended in poisoning by caustic copper or iron salts. In these cases it should be given in doses of 1.0–2.0 grms.

V.—MIXTURES AND COMBINATIONS OF IRON WITH OTHER METALS.

Iodide of iron, iron sal ammoniac and iron tartar are preparations belong-

ing to this group, and are superfluous. When two different agents are to be given it is better to give them separately, thus for instance giving sodium iodide and the iron separately.

1. Ferrum iodatum, iodide of iron, FeI, a gray scaly mass, which by the evaporation of its watery solution crystallizes in light green masses $FeI_2 + 4H_2O$. Is very easily decomposed. The pharmcopœia orders it to be prepared freshly at every prescription, the following being the formula: 3 ferrum pulveratum, 8 iodine and 18 aq. destillata, mixed while it is being warmed for so long a time, until the fluid takes on a green color. Such a solution contains 40 per cent. of iodine. For pills the above solution must be concentrated.

It is very properly supposed that this preparation produces the effect of the iron and iodine upon the body, and for this reason we would simply refer to what is said under iron and iodine.

Therapeutic Application.—The indications for the use of the iodide of iron have been constructed *a priori*. It ought to be of utility in those cases in which affections that are benefited by iodine are conbined with a considerable degree of anæmia. Such are above all scrofulosis and old cases of syphilis, in which the patients are pale, miserable and deteriorated. Also in chlorosis occurring in individuals who were formerly scrofulous; also in the series of conditions, more particularly in amyloid degeneration of the liver and spleen, which follow upon long standing intermittents, and are accompanied by considerable anæmia. Various observers are very much divided in their opinion of the actual utility of the iron iodide in these cases. Although formerly very much praised, the preparation has been recently considered to have very little advantage over other iron preparations, the majority considering it only an iron preparation as such, and nothing more. It is in fact impossible to arrive at a final conclusion in the face of so many differences of opinion; we have no comparative observations tending to show the relative value of simple iron preparation and the iodide of iron on the same diseases. We ourselves have seen no benefit result from its use in amyloid degeneration. We have not mentioned a series of other observations in which the iodide of iron is praised as a specific for various conditions, because most of these have a very ephemeral existence.

Dosage.—Since the preparation is very readily decomposed it is given in various combinations to obviate this difficulty in a measure. The simplest is the ferrum iodatum saccharatum, iron iodide mixed with milk sugar, 20 parts of the former to 100 of the latter, every 6 parts of the iodide of iron contain 1 part of iodine. From 0.1–0.3 (in children, 0.03–0.1) several times a day in powder, pill and troche, not very well in solution.

Syrupus ferri iodati, at first colorless, later on greenish, containing about 5 per cent. of iron iodide, from 0.2–1.0 pro dosi (5.0 pro die) in solution (by the addition of a few drops of acetic ether). In children 10–20 drops.

2. Ammonium hydrochloratum ferratum, iron sal ammoniac is probably not a chemical combination but only a mixture of sal ammoniac and a little iron (2.6 per cent.)

It is an orange yellow powder, readily deliquescing in the air and readily soluble, which is believed to combine the effects of sal ammoniac and iron. Therapeutically, entirely unnecessary, (0.3–0.5 in pill or solution, with succ. glycyrh.)

3. Ferro Kalium tartaricum—tartarus ferratus—iron tartar—A dirty green powder, which gradually turns brown, and dissolves in sixteen parts of water.

It is still used for the preparation of artificial iron baths, (50.0–100.0

grm. to a bath.) As to the utility of these baths compare what is said above, page 180.

MANGANESE.

In the organic world manganese is found associated with iron. So, also, in the animal organization, but here only traces are present in the blood, milk bile, urinary calculi and the hair. There is no evidence that it is an important constituent of these, not to speak of its taking any such part in the organism as iron does. The introduction of most of the salts of manganese, the citrate, chlorate and sulphate into the stomach is followed, according to Laschkewitsch, even without a simultaneous increase in diet, by an increased secretion of urine and urea, without any change resulting in the temperature of the body. Large doses of over 0.5 grms. produce gastro-enteritis, vomiting, and death by paralysis of the heart.

In very small but increasing doses, injected directly into the blood, symptoms of great bodily weakness and diminution in the force of the circulation occur, accompanied by fatty degeneration of the liver, and finally death from doses of 1.0 grms. Larger doses produce tetanoid convulsions and death from paralysis of the heart. This also follows the administration of the remedy internally.

In cold-blooded animals there is produced paralysis of sensibility, reflex irritability and voluntary movements; motor nerves and muscles are not affected (Harnack.)

These observations were made upon animals (rabbits, dogs and frogs,) and need further confirmation. They seem to indicate that the drug has a strong influence upon the heart and central nervous system, and thus show no similarity with the action of iron.

The following is the only preparation used medicinally, (for the other officinal preparation, manganum hyperoxidatum, is not thus used).

POTASSIUM HYPERMANGANATE—PERMANGANATE OF POTASH.

MnO_4K presents large rhombic crystals, which in reflected light appear dark and show a metallic luster, but by transmitted light are a purple red. It dissolves in sixteen parts of cold water, forming a violet red fluid.

PHYSIOLOGICAL ACTION.

It is a powerful oxidizing agent, and in this way destroys *most organic bodies*, being itself reduced, however, to a manga-

nous salt. To this oxidizing power over tissues all its physiological action is due.

Even in moderate dilution, it causes an inflammatory irritation of the skin, with intense, long-continued and burning pains. Strong concentrated solutions have a caustic effect. So, also, upon the mucous membranes, and for this reason it can only be administered internally in very strong dilution. The effects of such solutions are still unknown. In concentrated solution it would certainly produce severe gastro-enteritis, with all the resulting consequences.

Since it is a powerful poison for the lowest organism, and also on account of its oxidizing properties, it acts as a disinfectant and antiseptic. Its employment lessens the odor of the discharge in inflamed and suppurating wounds, and contributes to their healthy appearance and rapid cure.

THERAPEUTIC APPLICATION.

Although this agent is not used internally, it was very much used as a disinfectant a few years ago, and generally in those cases in which we now use phenol, and its allied substances: Foremost, it was used in the various putrefactive conditions; so also as a gargle in caries of the teeth; also as an application to ill smelling, suppurating surfaces, in gangrenous processes and ill-smelling lochia, etc. Not only does the odor disappear, but wounds thus treated take on a healthier appearance and heal sooner. Even if owing to the nature of the process a healing action does not take place, this remedy is still a very good one to remove the terrible odor of such a condition as cancer of the uterus and such analogous affections. If the permanganate be applied to wounds in too great concentration, it becomes painful and hæmorrhages occur.

Furthermore, the remedy is used as a purifying agent, and as such is used by physicians after examinations made upon patients suffering from a contagious disease, such as puerperal fever, syphilis, diphtheria, etc.

It is also used in the dissecting-room as a wash;—that it really removes the odor in such cases as the last is certain, but whether it really has the power of destroying the germs of contagious disease is yet questionable.

Potassium permanganate has also been used as a disinfectant for excrementitious matters, but apart from its questionable power in such cases, there is further objection to its use in its expense. It has therefore been proposed to use the soda-per-

manganate instead of the potash salt, which in large quantities can be prepared more cheaply.

Dosage.—Potassium permanganate—If it is to be given internally, it should be administered in from 0.05–0.2 grm., in solution, in distilled water, strongly diluted and without the addition of any other substance, since other materials readily decompose it. As a local application or mouth wash, we use a solution of from 0.5–100.0; as a purifying solution, 10.0–500.0. Externally, also, it must be given entirely alone; even cotton and charpie, when dipped into it, decompose it; the best agents for its application are bunches of asbestos, because this does not decompose the salt. The high price, however, prevents its general use.

MERCURY AND ITS COMPOUNDS.

PHYSIOLOGICAL ACTION.

Some of the compounds of mercury are soluble, and some are insoluble in water. The soluble compounds, when applied in the necessary strength, produce a caustic action at the point of application, while the insoluble compounds produce no local effect at all, or only so far as they are converted into soluble and new compounds in the organism. Although the local effects of the various preparations differ, yet all the soluble, as well as the insoluble compounds, have a similar general effect upon the animal body.

The only exceptions to this rule are those compounds in which the mercury is combined with a more energetic substance, such as the cyanide of mercury, in which the effect of the hydrocyanic acid preponderates.

The local caustic effect of the soluble mercury compounds upon the skin and mucous membranes, that of the mercurial chloride being the most powerful, is due chiefly to the action of these salts upon the albuminoid bodies, with which they form permanent and almost insoluble (in water) compounds. Like all escharotics, they loose their caustic effect in strong dilutions.

Action of the Various Mercurial Compounds Upon the Body.—The fact that even insoluble mercurial preparations are changed into soluble ones when they undergo absorption, would lead us *a priori* to the conclusion that both insoluble and soluble compounds present the same symptom grouping of chronic mercurial poisoning when used for a long time. Voit's thorough investigations have shown it probable that all of the mercury compounds are converted in the gastro-intestinal canal, under the influences of the sodium chloride, albumen, etc., into a *double* salt, namely, the chloride of mercury and

sodium, and into an albuminate, thus yielding the same "end products." So that the difference in the effects of the various preparations depends upon the difference in the time required by individual preparations to be converted into these salts, and upon the varying amount of preparations requiring the same time for this conversion.

Voit has divided these salts in three divisions, each of which yields different quantities of an active substance to the blood in equal periods of time. 1st group.—Ordinary mercury takes the longest time to yield a certain amount of mercury chloride to the blood; for this reason its action is very slow, but it is certain to produce the constitutional effect of mercury. 2d group.—Mercurous chloride, the representative of the sub-oxides and the salts of the sub-oxides, the mercurous bromides, iodides, and sulphates. 3d group.—Here the absorption is instantaneous; the chief representative is the mercuric chloride itself. To this class also belong the oxides and salts of the oxides, which are soluble in water, the mercuric bromide and iodide.

The final product of all these preparations is absorbed in combination with the sodium chloride of the gastric juice, as the chloride of mercury and sodium, $Cl_2 H_g + Cl. Na$—and then rapidly converted into an albuminate, by combination with the albumen of the blood. Mercuric chloride, as such, precipitates, as we have already stated, dissolved albumen. It cannot therefore be absorbed under this form, but this precipitate is dissolved both by albumen in excess and sodium chloride, both of which conditions are present in the blood, and to a certain extent even in the stomach. (Compare page 209.) If sodium chloride be added to an alkaline solution of albumen, no precipitate can be obtained by mercuric chloride; nor can even the alkaline reaction of this solution be effected, for the latter acts in a similar manner as a strong base to the albumen. The albuminate of mercury can only be decomposed by sulphuretted hydrogen, after the organic portion of this compound has been destroyed.

But since Mulder, Rose, Ellner and Voit agree that the mercury in this albuminate is in combination with oxygen (for all the chlorine can be separated by repeated washings), therefore we must consider that the chloride, when it combines with the albumen and sodium chloride to form a soluble combination, has already combined with oxygen; the molecule then *derived from all* the other preparations that finally circulates *in the blood is* the albuminate of the mercuric oxide.

When it has been used for a long time mercury can be found in all of the organs, such as the blood, liver, heart, brain, muscles and bones (Riederer and Overbeck). The duration of its stay in the body is various. According to one authority (Schneider), even a few weeks after the mercury treatment has been stopped, no trace of the metal can be found in the organs. Gorup-Besanez found it in the liver even after a year had passed.

It is excreted by all of the secretions. In the saliva, sweat, urine, bile and milk, in part, perhaps, as an albuminate. During the excretion of mercury the urine is often albuminous. According to Overbeck the liver is the chief organ of excretion ; the large percentage of mercury contained in the intestines is due to the bile which it contains. The excretion of reduced metallic mercury is improbable. The amalgamation of gold rings worn by patients suffering from mercurial poisoning, may take place by means of the excretion of any soluble mercurial salt in the perspiration (Voit), or even by the albuminate. The assertion that metallic mercury has been found in the urine must be received with the greatest caution.

Mercurials which have been internally administered and not absorbed, pass away with the fæces, especially if the compound have a cathartic action. But even that portion of the metal which has been absorbed and partly excreted with the bile, may thus leave the body with the fæces. In the fæces it is generally found in the form of sulphur compounds, which have been formed by combination with the sulphur of the sulphuretted hydrogen gas present in the fæces.

Riederer gave to a dog in the course of 31 days 2,789 grms. of mercurious chloride in 68 doses, from which the dog died. It appeared that of this the largest part, 77 % left the body with the fæces, and only 2 % with the urine. In the brain, heart, lungs, spleen, pancreas, kidneys, testicles, and penis, there were only 0.3 %, in the muscles 0.4, and in the liver 0.5 % of the mercury that had been introduced ; so that although only 0.09grms. of mercurious chloride had been administered, the amount absorbed into the blood was very trifling. In a second experiment also, only a slight amount was absorbed, but this was retained for a long time. If we compare the amount of mercury found in the different tissues, taking 1000. grms. weight of tissue as the basis for this comparison, we will find that in 100.0 grms. of fresh liver substance, there was 0.0066 grms. of the mercury ; in an equal quantity of brain *there was 0.0027* grms., in muscle, 0.0004 grms. So that liver

has relatively the largest and muscle the smallest amount of the metal.

GENERAL SYMPTOMS WHICH RESULT FROM THE USE OF THE MERCURIALS.

In the study of mercurial poisoning there is considerable confusion, since one series of observations were made upon those working in mercury, while others were the result of observations upon syphilitics. In the latter the symptoms due to syphilis were confounded with those which were the result of mercurials, which gave rise to confusion; some writers even supposing that syphilis was the result of the taking of mercury, which is certainly not true. Apart from this, the various effects of the mercury have not been represented as the result of the affection of various organs, but have been classified after the manner of works on natural history, as forty different diseases, or forms of diseases, (Dietrich, Falck), this classification being almost entirely untenable. Although we shall follow the critical and careful study of Kussmaul on constitutional mercurial poisoning, observed principally upon workmen in looking-glass factories, etc., we shall note, when necessary, the various points of difference between this and the form of more acute mercurial poisoning following the medicinal administration.

The rapidity and severity of the toxic effect varies with the person, preparation, and method of administration. It has the greatest effect upon young, ill-nourished, pregnant or unclean patients. The most terrible and purest forms of general mercurialism result from the inhalation of mercurial vapors. The effect of the stomach absorption is never so severe, since a large portion is immediately excreted by the bile and intestinal glands. Some individuals become ill very rapidly, while on the other hand there are workmen who have been employed in mercurial factories for forty years, and have never been affected.

Very large concentrated doses of soluble mercurial compounds cause severe inflammation of the digestive tract, and dangerous nervous symptoms. The medicinal administration of moderate doses, even, to workmen upon mercurials, produces the well known acute mercurial symptoms in the region of the digestive tract; inflammation of the mouth, salivation, gastric catarrh, *and diarrhœa.* The nervous symptoms which occur here are *only slight,* and rather secondary to the fever and digestive dis-

turbances. When the administration is suspended, complete health rapidly returns.

Small doses long continued give rise to chronic constitutional mercurial poisoning, slow but serious disturbances developing and the nervous system being generally involved. The nervous disturbances are sometimes preceded by the more acute affection of the digestive tract; they are characterized by weakness and increased irritability, often giving rise to a strong and almost convulsive trembling of the whole body. If the mercury is not suspended, an exhausting diarrhœa and disturbance of the nervous system will produce death.

The sequelæ of chronic constitutional mercurialism are as follows: the loss of single or all of the teeth, caries of the teeth, atrophy of the gums and of the alveolar margins, scars, and strictures in the first portion of the digestive canal, inflammation of the buccal cavity, hardening of the salivary and lymphatic glands, and gastric catarrh. On the part of the nervous system we have increased irritability, liability to fright, and fits of temper, pains in the limbs, sleeplessness, dizziness, attacks of unconsciousness, trembling, and weakness of the memory and judgment. In some cases the patient remains pale and lean. Some become fat but remain pale.

Influence upon the individual organs and functions.—Although the long-continued use of *small* doses of arsenic, phosphorus and antimony, is followed by characteristic pathological alterations of internal organs, as for instance the liver, spleen, kidneys, muscles and bones, mercury acts by preference upon the skin and mucous membranes, causing an alteration in these tissues, while the internal organs and nervous system are only affected by very large doses. The long-continued administration of small doses of mercury does not give rise to organic changes, although the symptoms during life might lead one to suppose that such was the case; if there be any such changes, they are inconsiderable and can certainly be healed. In favor of this view are the facts that mercurials can be continued for a long time and be well borne, and that even a great degree of "mercurialism" can be cured by suspending the drug, and proper treatment.

In the discussion of the general symptoms produced by mercurial poisoning we have given the chief organic disturbances, arranged chronologically.

Here we shall consider the functional disturbances of each organ in particular so as to gain a clearer insight into the individual *symptoms* of mercurial poisoning.

Skin.—Even the rubbing in of the ordinary gray ointment leads to inflammation of the skin. Beginning as an erythema it advances rapidly to eczema impetiginosa, or in some cases to severe forms of universal eczema. The soluble preparations, such as the chloride and iodide in certain concentrations, lead to the most violent inflammations of the skin, ending in mortication, and thus act as escharotics.

Even when internally administered, an inflammation of the lips, inner surface of the cheeks and throat, thus produced, can advance until it becomes erysipelatous, ending in phlegmon and even gangrene; and independently of all local action we have, as symptoms of general poisoning, eruptions upon the skin in the form of Roseola, Erythema, Urticaria, and Eczema. All of these forms of eruption are not in any way characteristic when present as symptoms of mercurial poisoning. The hair often falls out, but grows again. It certainly exerts no particular influence upon the sweat glands; just before death severe perspiration has been observed just as is the case in many fatal conditions; but mercury does not cause this. The sweating during Hg. cures is due to the warm envelopment in clothes, etc., warm rooms and similar causes, and not to the poison.

The digestive organs, as we have already mentioned, are always first and strongly affected. When the appetite has become affected a disagreeable metallic taste is always experienced by the patient; a foul odor issues from the mouth; the tongue becomes coated, swollen, and shows the impression of the teeth; the saliva is increased, the epigastrium swollen, and there is a feeling of pressure over the stomach, eructations and vomiting. Later on there is vomiting of food, mucus, and bile, severe abdominal pain, and diarrhœa alternating with constipation.

Often the inflammation of the mouth and salivation reach a dangerous degree. The gums and mucous membrane of the mouth and throat become red and swollen; the former are separated from the teeth, and bleed readily. The teeth are painful and loose, and between them and the gums there is a collection of a shining yellowish material.

The salivary secretion becomes very excessive, and the saliva runs constantly from the mouth. The patient cannot sleep because the saliva flowing into the larynx brings on attacks of dypsnœa. It has been said that 5 kilograms of saliva were collected from one patient in one day. This saliva is foul smelling and irritating; in the beginning its specific gravity is raised and later on diminished. Its reaction is strongly alkaline.

Then there are seen upon the mucous membrane of the cheeks, edge of the tongue, gums, alveolar margins of the gums, and tonsils, yellowish spotted sores, which are at first superficial but later on become deeper these soon spread and unite and advance until the maxillary bones are exposed; thus leading to periostitis and necrosis. Direct mercurial disease of the bones does not occur. The teeth fall out and the neighboring lymphatics swell. When the ulcers heal they leave stellate white cicatrices.

All of these affections of the mucous membranes are certainly due to the inflammatory and irritant action of the mercury; for that portion of the poison that has been absorbed is again excreted by the saliva, and thus is enabled to make renewed attacks upon the mucous membrane. The increased salivation is only partly the effect of the buccal inflammation; to a greater extent it appears the result of a direct influence, for increased salivation is found even if there is no inflammation of the mouth; there is always a mercurial compound present in the saliva. Since mercury affects almost all of the nerves it is possible that the cause of the enormous secretion is a direct irritation of the nerves of the affected salivary glands. The salivation is favored by the following conditions—want of cleanliness of the mouth, caries of the teeth, arrest of perspiration, cold, constipation and pregnancy; toothless children are least of all subject to it.

The symptoms on the part of the stomach and intestinal canal, depend upon gastro-intestinal catarrh and inflammation. The gastro-intestinal mucous membrane is often hyperemic and ecchymotic. Wunderlich has also seen large ulcers in the jejunum, Heilborn in the large intestine and cæcum, Lazarevic swelling of the solitary follicles and Peyer's patches as in typhus. This gastro-intestinal affection occurs also after the subcutaneous injection of mercury (Heilborn). The swelling of the epigastrium and frequent constipation appear to be due to paralysis or weakening of the gastro-intestinal nerves and muscles.

The accounts of all diseases of all possible glands, hypertrophy of the liver and spleen, hypersecretion of various abdominal glands, are either false, or to say the least unproved. Often this confusion is due to confounding the results of syphilis with the sequelæ of mercurial treatment.

Judicious and critical investigation has not yet shown any characteristic alteration of the glands, liver, spleen etc. Jaundice is a very rare affection in workmen using mercury in their art.

As to the excretion of bile there are contradictory individual observations. The swelling of the lymphatics of the neck is the result of the stomatitis and not of the mercury. After strong but not after weak subcutaneous injections of the sublimate, Heilborn found a hyperemia of the epiphyses and diaphyses; surrounding the vessels are found cloudy, red-colored masses and reddish cells tinted by the coloring matter of the blood. The fat cells of the marrow are often atrophied. Heilborn believes the pains in the bones occurring in mercurialized patients are due to the hyperemia in the marrow.

The excretion from the kidneys is as little altered as the perspiration. Some authorities speak of increased diuresis, but the assertion is not well founded. Overbeck and Lazarevic indeed, even speak of a complete drying up of the urinary secretion. The frequent but not constant albuminuria may be due to a catarrh of the uriniferous tubules. Kletzinsky, Saikowsky, and Rosenbach found sugar in the urine of mercurialized men and animals; perhaps in consequence of punctiform hemorrhagic spots on the floor of the 4th ventricle, as Lazarevic found them in mercurialized animals. Overbeck found lucin and a body similar to tyrosin as well as valerianic acid, while Saikowski found in the dilated urinary tubules of the rabbit a deposit of lime phosphate and carbonate. The mercury diabetes lasts according to Saikowsky for a longer time than all the other artificially produced forms of diabetes; (for 18 days).

General nervous system—Kussmaul considers mercury a cerebral poison. It is without doubt exceedingly poisonous to the general nervous system; especially if the drug be administered in very small doses.

A constant and prominent symptom of the cerebral trouble is a peculiar fright and embarrassment, which is present in a like manner in no other form of poisoning. Kussmaul considers this a strong proof of the influence of certain bodily conditions upon the finer mechanism of our disposition.

These constantly returning psychical disturbances produced by mercury increase until complete insomnia and anxious hallucinations are present, which sometimes, especially at night, lead to short maniacal attacks. Frequently attacks of dizziness, accompanied by falling and sometimes loss of consciousness, thus simulating epileptic attacks take place. But the assertion that real psychical disturbances, madness, and dementia occur as the result of the taking of mercury alone is unfounded.

In the course of time very frequently a condition sets in which the extremities or the muscles of the largest part of the

body are the seat of a violent tremor or even convulsive movements, during which the patient loses all control over his muscular movements and the body is thrown hither and thither. At the same time there is extensive muscular weakness, which often increases to a paretic condition, and the disease begins to simulate paralysis agitans. Such a disturbance of the organs of speech gives rise to stuttering.

Sensibilty is also often disturbed. Unbearable aching in the teeth, face and head, tearing and dragging pains in the limbs, a dull sensation in the breast and asthmatic attacks occur. Or we may have on the other hand paralytic sensory disturbances (paraesthesia); such as formication, and a feeling of numbness in the arms and legs; the æsthesiometer reveals anesthesia to touch and analgesia.

It is highly probable that the largest part of these disturbances are due to a direct involvement of the brain, spinal cord, and peripheral nerves, even if hitherto there has been found a dark discoloration of the gray substance in these parts, in only one case (Pleischl), according to Koch this was present in the white substance. There is no proof that any alteration in the substance of the muscle takes place. The electric muscular irritability is retained as Kussmaul found in a case of 7 years standing. The muscle shows an appearance of atrophy. The reflex irritability of the spinal cord remains unchanged being even sometimes increased. In favor of the cerebral origin of the tremor is the fact that we have at the same time other cerebral symptoms present, such as headache, dizziness insomnia and psychical disturbances; also the circumstance, that the tremor is often produced or greatly increased by the psychical disturbances; and finally that ordinarily the muscles of the face, then those of the arms and finally those of the limbs are attacked.

Respiratory Organs — The frequently observed difficult breathing and dyspnœa led Kussmaul to believe that the strength of the respiratory muscles becomes insufficient. Particular diseases of the lungs are not caused by mercury, but an already existing tendency to consumption may be increased by this poison. The fact that inflammatory conditions of the bronchi and of the lung tissue have been found in animals to whom mercury has been administered has not been well established; nor is it certain that these conditions were not present even before the mercury had been used.

Circulatory organs and the blood.—The force of the healthy human heart is very much diminished by the long continued

use of mercury—the pulse is rendered small and slow but every psychical disturbance increases its rapidity, hence there is frequent palpitation.

In patients in whom the heart was already weakened, that is to say in a condition of fatty degeneration, such a lowering of the blood pressure has been seen under the use of mercury that the stoppage of the heart was produced by the physiological diminution of irritability which takes place during sleep. The direct injection of dilute solutions of the chloride into the blood of frogs produced a rapid paralysis of the heart in diastole, before the remaining systems, such as for instance the nervous centers showed any sensible disturbances. In warm-blooded animals slight fatty degeneration of the heart has often been seen to occur.

We do not possess thorough examinations of the blood of patients suffering from mercurial poisoning. We should not therefore lay too much stress upon the various statements that the blood is poorer in water and albumen, or that the white blood corpuscles are increased in number, or that the disturbances produced by mercury depend upon anæmia. We cannot indeed deny that these patients do look very anæmic. But whether this anæmia is the direct result of the action of the mercury, or of the disturbed nutrition, resulting from the stomatitis, etc., is unknown. Outside of the body albuminate of mercury mixed with blood frequently causes a destruction of red blood globules. (Polodschnow.)

Temperature.—That mercury produces a rise in the temperature of the body is more than doubtful. As long as it does not give rise to inflammatory disturbances the temperature of the body remains normal; it is only in consequence of inflammation of the mouth, stomach and pharynx that fever sets in.

Organs of Generation.—In the old literature we find the statement that mercury, together with a mass of other remedies, increases the sexual desire. But since there is no standard for the amount of this desire, and since the desires of the males are very readily incited, we cannot give these assertions much credence. In females the menses become very much diminished, irregular, and sometimes disappear entirely. Very rarely they are increased, and become more frequent. Pregnant women show a tendency to abortion and premature labor.

Influence Upon the Interchange of Materials in the Body.—An impartial consideration of the action of mercury teaches that we must distinguish between its primary and secondary influence upon nutrition and the vital processes. The possi-

bility that for many years small quantities of mercury can be collected in the body without any disturbance in nutrition taking place, the fact that the first symptom, after many years of mercury administration, is generally a disturbance of the nervous system, such as the occurrence of tremor mercurialis, finally the duration of the so-called mercurialism for years, all these things point to the fact that mercury cannot have a very deleterious influence upon the vital processes.

In addition to this we have the fact that Boeck found that the excretion of nitrogen (in a syphilitic man who was under mercurial treatment), that is to say the decomposition of albumen circulating in the blood, was entirely unchanged and exactly as it had been before the treatment was begun.

The "anti-plastic, dissolving, melting and wasting" action ascribed to mercury by the older writers was the result of using very large doses in many cases, so that even at the very beginning a terrible grade of inflammation of the mouth and pharynx, gastro-intestinal catarrh and febrile symptoms set in; these diseases even when not caused by mercury always giving rise to disturbances of digestion and causing vomiting, diarrhœa and increased (febrile) oxidation of tissue. It is not possible to consider the mercury as the direct cause of the wasting and anæmia. When these local disturbances of the mucous membranes are prevented by the employment of all proper preventive measures (such as purifying the mouth, cleansing the teeth and a proper selection of the preparation and form of administering the remedy), the treatment can be continued for a long time without any disturbance in nutrition. We have convinced ourselves that syphilis treated by mercury in this way has resulted neither in loss of bodily weight, size or strength.

Theory of the Action of Mercury.—According to the older ideas the explanation of the action of mercurials was quite simple. Voit, for instance, explains all of the symptoms and effects produced by mercury in the healthy and sick subject by the formation of the albuminate of the oxide of mercury, which is with great difficulty decomposed. Upon this, he thinks, depends the slowness of excretion, since every molecule must be decomposed before the metal can be got out—eliminated from the body; upon this also depends its influence over certain "fermentation diseases," as for instance syphilis. The syphilitic poison on an albuminoid body combines like other albuminoid bodies with mercury, and thus loses both its separate existence and its poisonous properties. But with the poisonous substance healthy nitrogenous tissues are destroyed; it is like

bleaching linen—here the coloring matter is much more readily destroyed than the large mass of the linen; the result is that white linen remains behind, although a portion had to be destroyed in order to make the rest of the linen white. In syphilis it depends upon the relation of the infected to the non-infected albumen whether a cure is to take place. If considerable non-infected albumen still remains, then the infected portion will be destroyed, but a portion of the body must be sacrificed for this purification; all nutrition is disturbed.

In the present state of our knowledge it seems to us best to postpone any explanation of the action of mercury until we have better and more complete data upon which it may be founded. Under any circumstances the hypothesis of Voit is certainly not maintainable, although v. Boeck, in order to defend it as much as possible points to the organized albumen and ascribes to this the chief part in mercurial poisoning, as is shown by the disappearance of pathological conditions, such as condylomata under the influence of mercurial treatment. We ourselves, however, can only see from Boeck's examples that neither the albumen in the circulation nor that in the organized tissues undergoes any considerable change, but that syphilitic neoplasms do disappear. Would we not rather from this conclude that the *unknown syphilitic virus is the real point of attack of the mercury, and that sufficiently large doses of mercury destroy the syphilitic poison and its formations, while the normal tissues of the body are left almost or entirely* unaffected?

Choice of the Preparation.—Since all the preparations have the same physiological effect there appears to be no intelligent reason why we should make use of hundred different preparations to accomplish this action. Even Voit very properly proposed that for medical purposes only the three representatives of the above named classes of compounds should be used therapeutically. We shall carry out this proposition in the following section, and shall begin with the mercury chloride as the most important preparation. The irrational employment of this compound in pill form, by which means the caustic action of this compound is sharply localized, must be stopped, and instead the salt must be used in great dilution (0.001 grm. to 100.0 grm. of water), or it may be used as an albuminate internally (Baerensprung), or as a peptone (Bamberger), or it may be administered subcutaneously as the Hg chloride—sodium chloride. We believe that the last method will more or less replace all other ways of treating syphilis. Every patient (Bamberger) who was treated by hy-

podermatic use of the albuminates or peptonates increased in bodily weight, and did not suffer from salivation during the treatment, although no prophylactic measures had been taken. Even the internal use of the albuminate was not followed by any disturbances on the part of the stomach.

THERAPEUTIC APPLICATION.

Before specifying the various methods of application of the individual preparations, we shall first discuss the therapeutic action of all mercurials in general, or rather the effects that have been ascribed to them.

The mercurials are used in two different groups of diseases. In acute inflammatory affections of different organs and in syphilis.

The general application of mercurials in acute inflammatory processes was begun in the beginning of this century, although it had been previously used in trophic inflammations of the liver. Robert Hamilton (1805) was the first to recommend its use in this class of affections. Since then the best of the English physicians (Watson, Graves, Hope, etc.,) have been more or less in favor of this treatment. In Germany, mercury has been very little used in this way, and in France it has been even less used.

It is now of little importance to rake up old physiological theories to explain the utility of the mercurials in these inflammatory affections. As we have already, under the head of physiological action, shown, the "antiplastic" power "the power of facilitating absorption," the liquifying and "melting" power, all of these are mere wordy hypotheses, which our knowledge of the real physiological action of the drug has not confirmed, so that we have no real physiological grounds for using it in inflammatory processes. We can, therefore, judge of its utility only upon an empirical basis. What does this teach?

Every one who will take the most important literature of the subject into consideration will come to the conclusion that here diametrically opposed opinions exist. On the one hand, Hope asserts "careful and impartial observation has convinced me of the great efficacy and practical utility of this preparation in inflammation of the brain and other organs absolutely necessary to life." Hasse, however, in speaking of meningitis simplex, says "the innuction of mercurial ointments is frequently rec-

ommended, but I have never seen any good result from its use"; in tubercular meningitis he does not use it at all.

Altogether we may say that from the 30th to the 50th year of the present century, when mercurials were most popular, up to our own time, an increasing skepticism as to the utility of such an application of mercury has been manifested. Although at first applied in every possible inflammation it has been more and more limited in its application to certain well defined forms, so that to-day in Germany at least, mercurials are thought to be indicated only in inflammations of serous membranes. But even in pleurisy, pericarditis, peritonitis, and meningitis the impartial observer must recognize the uselessness of this drug in most cases. Apart from the tuberculous forms, in which almost every observer entirely denies the utility of mercury, daily experience teaches that the ordinary cases of meningitis, pleurisy, pericarditis and peritonitis run a favorable course without a centigram of any mercurial preparation being used. It is, therefore, now only used in those cases which run a rapid and very acute course. We ourselves, in the first editions of this work, expressed our adherence to this limited application of the drug, since we considered that in such very acute inflammations early and energetic mercurialization was, perhaps, the only means by which the process could be checked. We acknowledge that to-day even *this limited application can no longer be maintained.*

We have not yet seen any really indisputable evidence, that even the most energetic use of mercury diminishes or prevents the exudation or emigration of white blood-corpuscles in meningitis, peritonitis, etc. Besides, we must also consider that the other therapeutic means that are employed have some share in any effect that may be produced. Such are leeches, cold, etc. In such conditions an estimation of the mercury effect alone is impossible.

A classification of individual cases shows that the large majority of cases of slight and medium severity, run a favorable course without mercury, while the severest cases generally die in spite of the mercurial treatment, and even in those cases which do recover, it does not appear that a favorable change in the course of the malady followed the use of the mercurials. And how can we consider that in these few cases, the mercurials have produced this favorable result, when in many other analogous cases they were entirely inert. Nobody has yet been able to show that mercurials exert in fevers even an approxi*mately favorable* effect, such as follows the use of quinine in

large doses in certain forms of fever or malaria; or salicylic acid in acute articular rheumatism, or digitalis in certain forms of heart disease. If one chooses to administer these preparations because in these conditions nothing better or more certain is known we may do so; but we consider it better to state this openly, than to continue a therapy which is based upon an uncertain basis.

We shall here discuss the use of mercurials in puerperal fever, in which affection they were formerly much used, then discarded, to be again recommended by Traube in recent times. Since we ourselves have but little experience in the use of mercury, we shall base our conclusions upon the reports of others.

Mercury is of no use in those forms of puerperal fever which progress without any particular localization, that is to say, the pyæmic, ichorous, and thrombotic forms. But it is said to be of great utility in the phlegmonous form in which the inflammation of the uterus spreads to the coats of that organ and adnexa, whence it further spreads to the serous membranes such the peritoneum, pleura and in rare cases even to the pericardium. In the latter form of the malady it is said that the energetic use of calomel internally and gray ointment externally, together with other necessary therapeutic agents lead to a favorable termination of the disease. These patients can bear large doses, and it appears as if the favorable turn in the disease generally occurred with the appearance of salivation. According to the experience of Spiegelberg (Grossman) in an epidemic of puerperal fever, most of the cases presenting in the form of parametritis, a series of comparative observations distinctly showed a rapid decrease of the fever and diminution of the exudation produced by the administration of rapidly succeeding doses of the sublimate (0.01 grms. every one or two hours. All gynæcologists, however, do not entertain this favorable opinion of the power of mercury over this condition.

It has not by any means been positively determined that the mercurial treatment of croup and diphtheria is a very good one or that it is to be preferred to other methods of treatment. Indeed, according to all experience it appears to be without effect and injurious, even if the cases recover, on account of the general effect of the mercury. In ophthalmia of every kind mercury was used almost as a specific antiphlogistic, but recently it has been used only in iritis and especially the syphilitic form of the malady.

Apart from their use in these affections the mercurials are also used as antiphlogistics in a number of so-called surgical

affections and almost exclusively in acute inflammatory conditions of parts lying directly under the skin. It is applied in the form of gray ointment *ad locum affectum*. In what way the favorable influence of the mercury, which by the way can be doubted, is to be explained we do not know.

For this purpose we make use of inunctions of ung. cin. (gray ointment); these inunctions are to "dissipate" the exudations already formed, and to cause the whole affection to disappear. For this purpose, in addition to the ointment we use local blood letting, etc. To this kind of processes belong inflammation of the lymphatics and lymphatic glands, acute mastitis and orchitis, parotitis, myostitis, and acute diffuse phlegmon. Whether these affections can be thus influenced is indeed questionable, and surgeons doubt more and more the utility of this application of mercury.

Mercury has been used almost as a specific in syphilis. At first it disputed for the first place among the antisyphilitics with sarsaparilla, etc., but later on, during the last few hundred years it was used almost exclusively as an antisyphilitic. Not until recent times did the non-mercurial method gain the upper hand;—the controversy between the advocates and opponents of mercury is not yet finally decided, although the former exclusiveness has given way on both sides, and according to the latest reports mercury has again gained the upper hand. It is difficult to reach a final conclusion concerning a matter about which there are so many diametrically opposed opinions. But from the many contributions which we possess, on the value of the mercurials, we are able to reach the following conclusion:

In the first place we should premise that gonorrhœa and its local sequelæ being local diseases are not amenable to general treatment, and therefore do not need mercury. The same may be said of the ulcus molle (chancroid) and its consequences (suppurating bubos). Here we leave out of consideration the question whether a soft chancre can be followed by constitutional symptoms. As to syphilis itself, the hard chancre and the series of so-called secondary and tertiary affections, it is an undoubted fact that recent syphilis may, under favorable conditions, without any treatment, or only by the enforcement of dietetic regulations, run its course and disappear. Daily experience furthermore teaches that the spontaneous cure is furthered by the employment of agents that stimulate the natural modes of excretion—such as diuresis, diaphoresis, diarrhœa, etc. For this purpose we use the vegetable remedies, such as

sarsaparilla, etc. Of what value is this fact in the consideration of the treatment of syphilis by mercury? It is undoubtedly true that the use of this drug is often rapidly followed by a disappearance of all the symptoms of syphilis, much more rapidly than when we use only the expectant plan of treatment, or under the use of the vegetable infusions, etc., and it is this fact which gave to mercury its place as the foremost anti-syphilitic remedy. A cure generally follows the production of an acute mercurialism. All of the symptons do not disappear with equal rapidity, but the slighter secondary affections, such as roseola and condylomata lata disappear soonest, although even the severer grades of these take a longer time, while the primary indurated lesion is still more difficult of cure. Furthermore, mercury is of less utility in the tertiary symptoms, especially the affections of the bones.

But notwithstanding the real utility of mercury in syphilis, objections have been made to the use of mercury in the treatment of this disease; these are as follows: First, the possibility of treating syphilis without mercury; again, it is asserted that mercury does not cure the disease, but only renders the symptoms latent; furthermore, it is said that the use of mercury results in the appearance of serious tertiary affections; and finally that the system is more disturbed by the mercurialism than by the syphilis. We cannot here enter upon a thorough discussion of these points; but our impression is as follows: First, that it has been shown by many observers that the syphilitic symptoms have entirely disappeared after a single course of mercury, and that the patients have then enjoyed excellent health. So that for this purpose it is certainly the same thing whether the symptoms have only been rendered latent or the pathological process cured. On the other hand, it is just as certain that after the mercurial treatment the symptoms, although remaining latent for years, have reappeared in a more aggravated form. The third and fourth of the above objections are also not to be denied, but we must observe that tertiary symptoms appear even in cases not treated by mercury; and, furthermore, that these, as well as the symptoms of mercurial poisoning, have become very much rarer, since the *foolish and extreme* use of mercury has been rejected.

We arrive, then, at the following conclusions: That we can do without mercury in the treatment of simple forms of syphilis (roseola, condyloma, etc.), although these diseases disappear much more rapidly and permanently under the use of mercury. The *primary hard* chancre can indeed be made to disappear un-

der the use of mercury, but secondary affections are still apt to follow, so that it is better to treat the ulcus durum entirely without the employment of general means, in order not to weaken the system by a double "cure" carried on at the same time. A considerable number of experienced physicians (Sigmund, Zeisel, Laucereaux, Liebermeister, and others,) do not at present use the mercurials in the treatment of the primary lesion. Our own observations lead us to join their ranks. But we must remark that sometimes the dressing of hard chancres with the gray ointment is followed by rapid healing, and also a disappearance of the induration. In the tertiary stages mercury is less effective than iodine. Mercury, however, is indicated, and its use becomes imperatively necessary when the syphilitic symptoms attack an important organ. Thus, in iritis, in severe laryngeal affections, and sometimes in cerebral affections, a few observers, (as for instance, Baerensprung) deny its necessity in iritis. Sometimes cases occur which withstand even the most careful non-mercurial treatment; in these cases the symptoms generally disappear as soon as mercurials are used. Some observers maintain that even the tertiary symptoms, although less rapidly cured by mercury than by iodine, are more permanently removed by the former drug.

Experience has taught us certain conditions under which the mercurial treatment of syphilis should not be instituted at all, or only with great precaution. Among these is gangrene, or a tendency to gangrene of the lesion; also when serious digestive disturbances are present (internal use of mercurials); also when a decided anæmia or any other cachexia exists (provided such do not depend upon the venereal disease itself) such are scrofulosis, tuberculosis or a tendency to this condition, and scorbutic affections, especially of the mouth. We must also use it guardedly in chronic alcoholism. Pregnancy is a further contra-indication, but although our experience here is not yet conclusive, it is now the general opinion that a mercurial course can be very well undertaken up to the 6th or 7th month of pregnancy.

We do not exactly understand the way in which mercury influences the syphilitic process. Concerning this point we refer to what has already been said under the head of physiological action.

It was formerly believed that it was necessary to produce salivation in order that the mercury should be effective. This view, however, has been disproved by thousands of observations; so that now, on the contrary, it is sought as far as possi-

ble to avoid salivation; and to accomplish this many preparations and methods of preparation have been tried. We shall call attention to the advantages and disadvantages of each under the head of the individual preparations.

I. MERCURIC CHLORIDE—HYDRARGYRUM BICHLORATUM CORROSIVUM.

Mercuric chloride, $HgCl_2$ (corrosive sublimate) forms sublimed, colorless, transparent, crystalline masses of a sharply caustic metallic taste. It is soluble in fifteen parts of cold and two parts of hot water, but more easily in alcohol; it combines with many metallic chlorides to form double salts which crystallize from the mixed saline solutions; the most important of these combinations for us is that formed with sodium chloride $HgCl + NaCl + 2\ H_2O$.

The albuminate of this salt is best obtained by the aid of diluted and filtered egg albumen, which is added to a 5 % solution of mercuric chloride and a 20 % solution of sodium chloride mixed together, so that not all of the albumen is found in combination with the $HgCl_2$ while all of the albuminate is found in a soluble condition. Mercury peptone is prepared, according to Bamberger, in the following manner: We first prepare, as before, a 5 % solution of mercuric chloride and a 20 % solution of sodium chloride, then dissolve 1.0 grms. of meat peptone in 50 ccm. of distilled water and filter, and dissolve the precipitate in the necessary amount of sodium chloride (from 15–16 cc.) Pour the fluid into a graduated cylinder and add distilled water until the whole amounts to exactly 100 cc. The proportion of mercury is then 1 %, and every cc. contains exactly 0.01 grms. of mercury in combination as a peptone. The fluid remains quiet for several days. A small amount of a whitish floculent precipitate is separated which is then filtered. This solution can be kept much better than the albuminate.

PHYSIOLOGICAL ACTION.

Inasmuch as the local and general effects of this soluble preparation have already been treated of under the general discussion of mercury, we may limit ourselves here to calling attention to a few of its especial peculiarities.

Mercuric chloride, like most of the soluble metallic salts, is a powerful disinfectant, and is fatal to the lower organisms (bacteria), even in strong dilution (1–20000 according to Buchholtz), so that it is ten times as powerful as thymol and the benzoate of sodium, twenty times as strong as creosote, oil of wild thyme, carvol, and benzoic acid, thirty times as powerful as salicylic acid and eucalyptol, and one hundred times as powerful as carbolic acid and quinine. It is only second to chlorine among the antiseptics with which we are familiar.

In regard to its relation to albumen, and artificial digestion, the later observations of Marle give the following facts: That from the behavior of Hg. chloride in the presence of alkaline solutions of albumen, we cannot draw any conclusions concerning its behavior in the presence of acids, for the relations of the

latter are exactly the reverse of the former. While the Hg. chloride, sodium chloride of Voit* produces a precipitate only when there is an excess of sodium chloride in alkaline solutions of albumen, Marle finds that in acid solutions of albumen Hg. chloride alone produces no cloudiness or precipitate, but these are produced upon the addition of sodium chloride; furthermore, that the deposit produced by Hg. chloride in alkaline solutions of egg albumen immediately disappears upon the change to a slightly acid reaction. It is therefore even irrational to administer much sodium chloride with the Hg. chloride given internally, because it only increases the power of the Hg. chloride, in the acid solution of the food in the stomach, to interfere with digestion. On the other hand, the hypodermic injection of Hg. chloride is certainly not as good as the injection of the Hg. chloride, sodium chloride with an excess of sodium chloride, because the latter is an alkaline solution.

If a medicinal solution of Hg chloride (0.03 %) be added to a fluid undergoing artificial digestion, it does not throw down the peptones, even when no sodium chloride is added; and if the concentration of the solution does not exceed 1 %, the pepsin is also not deposited. But yet the Hg. chloride decidedly interferes with the process of peptonization of the albuminoids when added to solutions undergoing artificial digestion, even in small doses, and Marle explains this by the formation of the soluble albuminate of mercury, which can be formed in acid solutions also, and which enables it to withstand the action of the pepsin. That the disturbing power over digestion which Hg. chloride possesses is increased by the addition of considerable amounts of sodium chloride is to be inferred from the fact that sodium chloride has a shriveling effect upon Hg. albuminate.

In very small doses or in considerable dilution, or when administered internally as an albuminate, the Hg. chloride is very well borne in the higher animals and men, without any disturbance of the appetite, and according to some, even with an improvement in the appetite. Among all the mercurials it is the last to give rise to salivation and affections of the mouth, while it is one of the best preparations for the production of the general and healing effect of the mercury.

When injected hypodermically in small doses as a double salt, albuminate or peptonate, it does not produce any local irrita-

* Compare page 192.

tion, provided that the solution that is used is a clear one. (Bamberger, Stern.)

In very dilute solutions it may be used in the form of baths; in such dilution it does not produce any local irritation, is not absorbed by the whole skin, but is absorbed by the ulcerated skin and those portions of the mucous membranes which are exposed, thus producing hydrargyrosis.

We see then that Hg. chloride, in small medicinal doses, strongly diluted, produces no evil local affections of the skin or mucous membranes; but these certainly do occur when it is given at once in too large or too concentrated doses.

Moderately concentrated solutions produce inflammation of the skin, while strong concentrated solutions act as escharotics and destroy the tissues, a similar effect is produced upon all the mucous membranes of the digestive tract when these solutions are taken internally. Especially is this the case with the gastro-intestinal inflammations, which attain such a height that the symptoms resemble those of arsenic poisoning or an attack of cholera, and either cause death or a series of very serious sequelæ, such as fibrous strictures, etc, Kalman noticed in the rabbit even nephritis with degeneration of the epithelium.

The older physicians appear to have been of the opinion that the mucous membranes could be gradually accustomed to the administration of larger and larger doses, and therefore recommend in mercurial treatment a gradual increase of the dose of the medicine. The so-called Dzondi's method for example increases the dose from 0.0003 grms. to 0.1. grms, which is ordered to be prescribed in pill form. This opinion is just as ridiculous as would be the idea that the human body would not be burned by fire if the temperature were raised to the burning point gradually. *The animal body cannot become accustomed to a caustic. When a certain dose and concentration are attained, an escharotic action follows, whether the organism has become accustomed to smaller doses or not.*

That Dzondi's method did not do more harm is only due to the fact that a large portion of Hg chloride underwent decomposition in the pill, and furthermore, because the pills were generally given immediately after meals, so that an albuminate was formed with the albuminous contents of the stomach.

It is not true that Hg. chloride exerts a specific action different from that of other mercurials upon the lung, as in bronchitis, pulmonary hæmorrhage or tuberculosis.*

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* See page 199.

THERAPEUTIC APPLICATION.

Formerly the corrosive sublimate was recommended in a large variety of conditions (neuralgias, exanthemata, pneumonia, etc.) In none of these is it of any use, and we shall therefore not go into a detailed enumeration of these. As an anti-syphlitic, however, it has a great reputation, and was even formerly considered the best of the mercurials for this purpose. Other observers, however, consider that no other preparation is so uncertain and slow.

The fact is that no other preparation so quickly disturbs digestion, as the sublimate, especially when given in pill form, while no other takes so long to produce mercurialism, and especially salivation. It was much used in certain manifestations of syphilis (affections of the bones, neuralgias, etc.), according to certain methods of which Dzondi's is the most widely known, although not the best. Lately the subcutaneous method has again brought corrosive sublimate into use. This method has the advantage of enabling us to dose the drug more accurately, and furthermore we can in this way, by large doses, most rapidly produce the general effect of the mercury, a matter which is of great importance in the treatment of some of the manifestations of syphilis, such as iritis. Some observers however do not believe that corrosive sublimate has this latter power. Lewin also believes that no other method is followed by so few relapses as this ; but other observers do not agree with him. The disadvantages of this method are the pain produced in many cases by the injection, which may be somewhat alleviated by the addition of morphia to the solution, and the danger of producing inflammation of the skin, abscess and even gangrene at the point of injection. We, ourselves, however, have never seen either gangrene, dermatitis or even any considerable pain, follow the injection of the Hg. chloride—sodium chloride solution as prepared according to the directions of E. Stern and S. Müller. Some have not observed any advantages from the employment of the subcutaneous method, especially in the duration of the treatment, concerning which point opinions vary very much.

But this method has certainly several undeniable advantages, such as the fact that it does not disturbed the stomach while the dosage can be easily regulated, its effect also is very rapidly produced.

Whether the use of the murcury peptone as recommended *by Bamberger* has so many advantages, that it should be pre-

ferred to all other preparations, must be determined by experience. This method of subcutaneous injection certainly seems to produce the least amount of pain and local irritation; but the great difficulty in the application of it lies in the fact that only a clear solution can be used. But since, as we can testify, the mercury chloride—sodium chloride, recommended by Stern and Müller possesses the same advantages as the peptonate, the former will perhaps take the place of the latter. Corrosive sublimate baths are entirely without effect in adults but said to be of great utility in children for pemphigus neonatorum and in pustular eruptions.

Externally corrosive sublimate is much used. First as a wash for freckles and acne; also in pityriasis simplex and versicolor. It acts in these conditions like other remedies, *e. g.* potassium carbonicum, by producing an irritation of the skin; whether it has any advantage over other remedies we cannot say. Solutions of this drug are also useful in prurigo whether of the circumscribed (pr. pudendorum) or general variety; in the former it is used as a wash, and in the latter in the form of baths. But the use of these solutions is contra-indicated when there is a severe inflammation of the skin (in consequence of scratching).

Corrosive sublimate was formerly more used than it is now in purulent ophthalmia. At the present time other astringents, such as nitrate of silver and zinc, are preferred. It is no longer applied as a counter-irritant to sores, &c., but Bergmann uses corrosive sublimate gauze in the same conditions in which he would apply carbolized gauze or cotton. As a local dressing to syphilitic condylômata calomel is to be preferred.

Dosage and preparations.—1. Hydrarg. bichlor. corrosivum internally from 0.005–0.01–0.03 (0.03 pro dosi ! ad 0.1 pro die !) best given in solution in water (strong dilution) or in solution with an egg (0.1 hyd. corros. to 150.0 of water with an egg). In the Dẓondi's method, mentioned above 0.75 gram. of corros. sublimate are dissolved in water and mixed with mica panis and saccharum aa q.s ad 240 pills. Of these pills 4 are given the 1st day, 6 the 3d, 8 the 5th, etc., up to 30 pills per day. During this treatment the diet must be sparing, meat without fat is given in moderate quantities, and milk entirely prohibited while the pills are taken; above all the room must be maintained at an even temperature. The pills should be taken a quarter of an hour after meals. The dosage for subcutaneous injection is the same as that for internal administration; either a simple watery solution is used or the mercury chloride—sodium chloride or mercury peptonate. We generally use a solution of 0.2 H. bichlor. corros. and 2.0 sod. chlorid. in 50 of water (Stern and Muller). Externally 0.1–0.2 per cent. solutions are used; for eye washes 0.05 per cent. solutions. *For baths 5.0–10.0 grms.* for one bath. For a bath for a child, we use

according to age 0.1–2.0, the bath to last a half hour. As an ointment 1 part to 24 of ung. simplicis.

* 2.—Hydrargyrum bichloratum peptonatum can be best ordered in the following manner: ℞—Hydrarg. bichlor. corros. 1.0—solut. pepton. aquos. 50.0—sodi. chlor. q. s. fiat solutio—filtra D. S. A hypodermic syringeful thus contains 0.02 of Hg.chloride.

* 3.—Corrosive sublimate gauze—ordinary gauze is deprived of its fat by boiling with lye and washed until all of the alkali is separated from it (until the water is no longer alkaline in reaction), it is then dried, and soaked in a ½ per cent. solution of corrosive sublimate (hg. bichlor cor. 7.5—spir. vini 1000.0, aq. dest. 150.0 and glycerine 500.0). It is allowed to remain in this solution for half an hour, then wrung out, but not too dry, and packed while still moist. This solution is sufficient for 3 klgrm. of gauze.

4.—Aqua phagedenica—phagedenic water—1 part of corrosive sublimate with 300 parts of aqua calcaria, used as a dressing in syphilitic effections.

2—MERCUROUS CHLORIDE—HYDRARGYRUM CHLORATUM MITE.

Mercurous chloride, Hg Cl or Hg_2Cl_2 (calomel); obtained by sublimation from a mixture of 4 parts of hg-chloride with 3 parts of metallic mercury. It forms a yellowish transparent, fibrous mass, which is tasteless and odorless, and entirely insoluble in water, alcohol and dilute acids. Under the influence of light, metallic mercury is separated and it turns gray, it should therefore be kept in dark bottles.

It is obtained, however, in an especially pure and finely divided state when the vapor of the above preparation is condensed by contact with the vapor of water (steam). This preparation is distinguished from the first, in the German pharmacopœia by the name hydrargyum chloratum mite. vapore paratum.

PHYSIOLOGICAL ACTION.

Buchheim and Oettingen believe that the mercurous chloride is changed in the body into the albuminate of mercury; concentrated solutions of sodium chloride have indeed the power of converting small quantities of mercurous chloride into the mercuric salt, but in the stomach there is too little sodium chloride present, to produce even a partial change of this nature. Voit, however, as we have already stated, believes in the possibility of the formation of the mercuric chloride, for when the mercurous chloride is placed in contact with solutions of albumen, metallic mercury is separated, which Liebig considers an evidence of the formation of the mercuric chloride. However this may be, mercurous chloride certainly does, in spite of its insolubility, undergo some change in solubility which renders it absorbable; for small doses 0.005–0.01 grms. continued for *some time*, often produce acute mercurial symptoms such as

stomatitis and salivation (more difficult in children) more rapidly than any other preparation.* Upon what this very prompt effect upon the salivary glands, which calomel produces, depends, we do not know. And this is the more difficult of explanation because only small proportions of calomel undergo absorption, the larger portion of even small doses passing out of the body with the fæces. (Riederer)† Salivation has been known to follow the administration of doses amounting altogether to 0.1 grms.

Larger doses, of 0.1–0.5 grams. frequently repeated, are followed very rapidly and generally without pain, by thin fluid passages, in which are seen many of the products of pancreatic digestion such as peptone, leucine and tyrosin. (Radziejewski.) The mercury thus administered in the shape of cathartic doses of calomel is not absorbed but all of it passes out with the stools, so that calomel thus administered acts as a cathartic.

The thin fæcal masses, which sometimes appear as though finely chopped, are, in children especially, of a characteristic grass-green or dark color. Most of the older writers, and also Buchheim, think this color depends upon the large percentage of bile contained in these fæcal masses. The latter observer extracted the dark coloring matter of the fæces by alcohol ; and the extract thus obtained gave all the reaction of bile. In the residue was found the sulphide of mercury, to which the more recent authors ascribe the above mentioned dark color ; the sulphide, however, was not evenly distributed throughout the mass, and its quantity was so small that it would hardly suffice to color the whole mass. Although in contradiction to Buchheim's view it might be said that under the use of calomel the tongue also sometimes shows a green color due to mercury sulphide (Traube) and that even normal fæcal masses when mixed with calomel become dark in color, yet these facts do not disprove the results of Buchheim's experiments. It does not, however, follow that because the characteristic color of the stools is dependent upon the bile, calomel increases the biliary secretion. The experimenters upon animals (Kölliker, and H. Müller, Scott, Bennet and Radziejewski) found in dogs with a biliary fistula that calomel caused either no change or a diminution in the biliary secretion, indeed the latter fact is proved conclusively to be the case in dogs by

* See page 194.
† See page 193.

Rutherford. But even for the solution of this point, more accurate observations are necessary, since Buchheim has positively found that the bile is sometimes increased. We must distinguish between the secretion and excretion of bile. For we can imagine an increased excretion of bile into the intestine taking place, while the secretion is really diminished, as when the biliary passages are cured of a catarrh or plugs of mucus are cleaned away, leaving the canals free (H. Köhler).

Frequently enormous doses are borne by the stomach without producing any other effect than diarrhœa. But there have been cases in which violent gastroenteritis has been produced, similar to that resulting from large doses of corrosive sublimate. In these cases also diphtheritic sores have been found in the large intestines. Riederer saw the administration of even medium doses to dogs followed by ecchymoses into the gastric mucous membrane, which, in the neighborhood of the pylorus, formed large plaques and gave rise to bloody passages, all these facts speak in favor of Voit's theory of the conversion of the chloride into the bi-chloride. Th. Kölliker very rarely found that the subcutaneous injection of calomel was followed by stomatitis, salivation, digestive disturbances or eczema, although it exerted an antisyphilitic effect.

THERAPEUTIC APPLICATION.

Calomel is one of the most commonly used drugs. Indeed by some physicicans and in some localities it is even misused. Since, as we have remarked, it produces the general mercurial effects very quickly, it (as well as the gray ointment) has always been very popular, especially if the mercurial effect is to be produced in inflammatory conditions. We have already expressed our opinion concerning the value of mercury in inflammation, and shall not here repeat. However even in acute trophic forms of hepatitis, according to Budd, Annesby, and others, calomel is only useful in laxative doses.

In syphilis also, calomel is the most used of all the mercurial preparations, and it can not be denied that it is to be depended upon while it has the additional advantage of being well borne by the stomach. But it readily produces salivation and diarrhœa; to prevent the latter, it is often given in combination with opium. In syphilis of pregnant women and new born children, calomel is preferred. Concerning the hypodermic injection of calomel, see page 219.

The most characteristic property of calomel as compared with

that of other mercury compounds, is its laxative effect. It is to be preferred to castor oil, in that it can be given even in inflammatory and ulcerated conditions of the bowels. Like castor oil, calomel is to be used when a single action of the bowels is required, and is not used, in Germany at least, in chronic constipation. Much has been said of, and it is to-day the common opinion that, calomel as a laxative has a "specific" action. It is generally given in inflammatory conditions of various organs in which a cathartic is indicated. It appears to us, however, that the especial superiority of calomel as a cathartic in inflammatory affections has not been shown even in the remotest manner. Indeed according to our own experience we are inclined to believe that even in abdominal typhus, when a laxative is necessary, castor oil is as useful as calomel, and as to a specific abortive effect of the latter, we do not believe that calomel has any such power. Calomel has doubtless its advantages as a cathartic, but these consist, we repeat it, in the fact that it can be given, like castor oil, even in inflammatory states of the intestines, and that it is even superior to ol. ricini, in that it is better borne by the stomach.

The idea that calomel should be given as a cathartic when we wish to act upon the biliary secretion, is, as we have shown above, not well founded physiologically. Practically we have been unable to convince ourselves that the preparation has a "cholagogue" effect, and that it should therefore be preferred in icterus and other disturbances of the liver. That in these conditions it is often indicated on account of the presence of a gastro-intestinal catarrh is of course another matter. It is rarely used by us for simple constipation, but in England and North America it is one of the most common remedies for this purpose, and generally in combination with jalap.

Calomel as a rule has an excellent effect as a cathartic in small repeated doses in the diarrhœa and vomiting of very small children, which so often occurs in the summer as a result of digestive disturbances. Although the utility of the calomel in this affection is from time to time doubted, yet it can not be entirely denied, for there exists a great deal of evidence in favor of this view, and our own experience confirms it. We do not suppose that even in these cases it acts in any other way than as a laxative, but for these cases we have no other fitting laxative. Calomel has been given in cholera according to various methods and doses (even up to 5 grms. pro die) with the idea of exciting an increased secretion of bile (although *this method would* not be of any use, even if we were to

acknowledge that this is one of the physiological effects of calomel). The study of statistics will lead to no positive conclusion, because the character of the disease varies so much in the different epidemics. But this much appears evident, that the percentage of mortality is no less under the calomel treatment than with the other methods. Much has been said concerning the calomel treatment of abdominal typhus. Formerly it was given with the idea of aborting the disease at the outset, but the idea has long since been given up. Experience has taught us that when calomel is given in recent cases there is a slight alleviation in the severity of the affection, and remittance in the fever, as soon as the movements from the bowels set in. The conditions under which it should be administered are that the disease should be in the first stage (up to the ninth day), patient strong, intestines but moderately affected, and fever considerable ; 0.5 should be given two to four times in 24 hours. We have already said that even here the effect is to be explained by the cathartic action of the drug.

Externally, calomel is used as a mild irritant in a variety of conditions. It is dusted into the eye in opacities or cloudiness of the cornea.

It should be preferred to other more active remedies, when the opacities are quite fresh and have not yet lost all of their sensitiveness. Leber and Schlaefke recently again call attention to the fact that this calomel dusting must be suspended, while the potassium iodide is given internally or has been given one or two days previously. The reason of this is that the calomel may combine with the iodide of the tears to form mercuric iodide, which, as observations have shown, may produce severe ophthalmia. In chronic sores, as for instance broad condylomata, etc., calomel may be used locally. It is a fact that condylomata which have lasted for some time in spite of general treatment, undergo softening when dusted with calomel, (having been first wet with salt water). Subcutaneous injections of calomel, as recommended by some observers for general syphilis, are said to produce a more thorough and longer enduring effect ; but this method gives rise to abscesses very easily.

Dosage and Preparations. Hydrarg. Chloratum Mite.—To produce the general mercurial effect we give 0.00 5–0.1 several times a day; *as a laxative,* 0.2–0.5–1.0 (in children, 0.01–0.1), best given in powder *or pill ; it is often* combined for this purpose with other remedies, such as *jalap and rhubarb.* If it is to be continued for some time, as in syphilis, it

should be combined with opium (0.05 calomel with 0.015 opium, 3 times a day in powder). As a powder it is used under its own forms. As an ointment, 1 part of calomel, 10 parts of adeps. For subcutaneous injection, 0.05–0.1 for a dose, suspended in glycerine and water; injection to be repeated every 5 or 6 days.

2. Aqua phagedanica nigra, s. aqua nigra, s. mercurialis nigra, liquor hydr. chlor. mit. cum calcaria usta—black wash, 1 part of calomel, 60 parts of aqua calcaria, as a wash for syphilitic affections.

3.—GRAY MERCURIAL OINTMENT—UNGUENTUM HYDRARGYRI CINEREUM.

Rub 6 parts of purified mercury with 1 part of old gray mercurial salve, until no globules of mercury are any longer visible; then mix with 4 parts of talc and 8 parts of lard, which has first been melted, then cooled. The ointment should have a bluish gray color.

PHYSIOLOGICAL ACTION.

The investigations of Voit and Overbeck prove that fresh gray ointment is simply a mixture of finely divided mercury and fat. But when kept for a time it contains very variable quantities of sub-oxide of mercury in combination with a fatty acid, which is formed while the fat of the ointment becomes rancid. Voit reckons that 1 grm. of mercury is mechanically subdivided into about 152 million globules by being rubbed up with the fat, and that the superficies is thus increased 534 times.

As to the manner and means by which the mercury is absorbed into the body by the inunction of this ointment, opinions of different experimenters vary. Oesterlen, Voit, and especially Overbeck, assert with great positiveness that they have seen most minute globules of mercury in the meshes of the skin and subcutaneous connective tissue; also that they have been seen in all of the organs, urine and fæces, either unchanged (Overbeck) or partially oxidized (Voit). This occurred in spite of extremest precautions that the mercury should not directly reach the mouth and stomach either by being sucked up by the tongue of the animal or by being introduced into the mouth (in men) by the hand which had handled the mercury. Donders, Baerensprung, Hoffmann, V. Recklinghausen and Rindfleisch on the other hand deny with equal positiveness that metallic mercury can be absorbed through the unbroken skin and thus reach the fluids of the body. Furthermore, while Baerensprung firmly believes that the salt of the sub-*oxide and fatty* acid alone is the active ingredient of the

gray ointment, and Buchheim also considers the ointment of the sub-oxide of mercury more active than that of the metal, Overbeck, led by direct experiments on the subject, believes that the latter are certainly not weaker than the former.

We ourselves believe with Kirchgässer that in the ordinary method in which this ointment is applied, the mercury is absorbed less through the skin than through the respiratory organs. For it is positive that metallic mercury, even under ordinary temperatures, and more so under the influence of bodily warmth, and the extraordinarily fine subdivision of the metal upon the skin, does undergo vaporization. This vapor rises under the clothing of the patients, saturates the whole of the surrounding air and is thus taken into the mouth and nose and inhaled into the lungs. It has been shown, however, that many other substances in the form of vapor or gas are taken up by the unbroken skin, and it is perhaps possible that mercurial vapor is also, even if the globules do not thus enter the blood. But even the latter can possibly be absorbed, if in consequence of the inunction there be an inflammation of the skin, formation of vesicles and perhaps an eczema, so that the skin is deprived of its epidermis in certain localities. This fine vapor of mercury may thus travel through the blood and tissues of the organs, partially oxidized under the influence of of the sodium chloride, the albumen of the blood and organs, and the acid of the blood corpuscles, and partly unchanged, to reappear in the secretions and excretions as metallic mercury.

It is well known (Schiff, Triumpf) that men and animals, who live in rooms in which mercury lies exposed and vaporizes, or in which others are being subjected to the inunction cure, are as apt to suffer from general acute and chronic mercurialism, as those upon whom the inunction is practiced. The constant and direct contact of the vapor of mercury with the mucous membrane of the mouth, explains why it is that the inunction method is so rapidly followed by stomatitis and salivation.

From what has been said it will be seen that to retain the gray ointment among our therapeutic agents, is against every rule of rational pharmacology. It appears right to drop this preparation from the list of mercurials. We were led to place it among the more important mercurial preparations, not so much on account of its antiquity (it having been medicinally used as far back as 1,000 years ago), for this would be rather a *reason for* dropping it, but because it is still one of the most *popular* mercurial preparations. And yet one of the first laws in therapeutics, that the physician should know the exact dose

administered, when a powerful drug is used, is set at naught when the ointment is used. We can never know exactly how much mercury has gained entrance into the body, nor how much of that which has been absorbed, undergoes oxidation, and thus exerts any effect. In the inunction cure the largest part of the mercury is lost and only small quantities are absorbed. Now, we ask, what sense is there in using a preparation of which 99 parts are wasted and 1 part absorbed. Again, the application of this method is unclean and very inconvenient. In this respect it can be compared with no other remedial agent, with the exception, perhaps, of mud baths. Finally we have not even the advantage by this method of application of avoiding the stomatitis or salivation, for, as we have said, the use of the gray ointment is very apt to be followed by both of these symptoms. The only use of this preparation which seems justifiable is as a local application to some of the forms of chancre.

THERAPEUTIC APPLICATION.

Without entering upon any special discussion of the application of the gray ointment, we shall only refer to what has already been said of the indications for the use of mercury in general. Unguentum cinereum has always been very much used for the production of mercurialization, either in syphilis or the acute inflammatory affections, especially when it was desirable to bring the organism rapidly under the influence of mercury. As to the necessity or rather the superfluity of this preparation for this purpose, we have said enough.

A further application of the gray ointment is as an *antiparasitic*. It is positive that mercury does not kill the itch mite, and is therefore not used in scabies. But it is a trustworthy remedy against head and crab lice. The inunctions should not be continued for too long a time, lest a disagreeable mercurial eczema, or perhaps general symptoms should set in. Blasius, Volkmann and others also recommend the unguentum cinereum as an aid to the cure of lupus; sometimes it exerts in these cases excellent curative effects. In some forms of croupous inflammation of wounds having a tendency to take on a diphtheritic action, Volkmann recommends this ointment as a dressing. As to its utility when locally applied to hard chancres, compare page 208.

Dosage and Preparation.—1. Ung. Cin. As a parasiticide a piece the size of a pea should be taken and well rubbed in. For antiphlogistic purposes,

2–5–10 grms. are applied daily, the quantity being divided among several inunctions. In energetic mercurial treatment, as for instance in puerperal fever, the most common method is to use every hour alternately 0.05 calomel and inunctions of 1.5 ung. merc. In the methodical inunction "cure" the location of the inunction should be changed from time to time in order to prevent eczema; and it is best to select parts of the body where the skin is tender, such as the bend of the elbow and the inner surface of the thigh. The inunction is best carried out with a piece of leather or linen. The inunction cure of syphilis has been systematized and is of two varieties, the greater and lesser cure. The former (the inunction method of Rust and Louvrier) is no longer used, because it weakens the patient, besides being no more effective than the lesser cure; we shall therefore not describe it in detail. The milder method of which we have just spoken consists first of 5–10 days preparatory treatment during which the diet is limited and water baths are taken. After this 2.0–4.0 grms. are rubbed into the body, in locations where the skin is delicate, every evening, covered, and then washed in the morning. The diet should be sparing and mild. The room may be aired and the underclothing changed. The inunctions are continued until the symptoms disappear. Not infrequently salivation sets in. The teeth and mouth should be kept clean by washing with solutio kali.

2. Emplastrum hydrargyri, E. mercuriale—8 parts mercury, 4 of turpentine, 24 of emplast. plumbi simplex. and 6 of wax, has a gray color. Used for local purposes when a general effect is not desired.

4.—METALLIC MERCURY. HYDRARGYRUM DEPURATUM.

Mercury is a silver-white metal, heavy, fluid at ordinary temperatures and without taste or odor. It gives off a vapor even without being warmed.

PHYSIOLOGICAL ACTION.

When the animal body is subjected for a long time to the influence of mercurial vapor, as is the case with those employed in mercury factories, and in those where mirrors and thermometers are made, as well as amongst gilders, the acute and chronic symptoms described in the introduction as characteristic of mercurial poisoning set in.

When ordinary mercury, however, is administered internally in large quantities, it gradually passes off rapidly with the fæces, since the dragging of the stomach and intestines caused by its weight produces increased peristalsis. Since it is not absorbed, it can not produce any general symptoms of poisoning. Were it retained in the stomach for a considerable time, its vapor or products of oxidation might be absorbed into the blood and thus produce the symptoms of mercurialism.

THERAPEUTIC APPLICATION.

Metallic mercury was formerly administered to remove *simple, persisting* obstructions; but at present it is used only in

ileus. It was given in this affection without any regard as to the anatomical condition that might be present in any individual case. It was used with the idea that by its weight it would cause imprisoned or involved folds of the intestine to be pulled back, or portions of the gut which were telescoped from below to be pushed out. Experience has taught us, however, that mercury should be used in ileus only as a last resort, when all other means have failed and operation is denied, because its administration is accompanied by several dangers, among which tearing of the inflamed portions of the intestine is one. It should not be used at all in external herniæ (because here better means are at hand) nor in intussusception, because even if the metal should reach the affected portion of the intestine, it might just as likely cause the intussusception to be increased, certainly it should not be used when inflammation of the intestine is suspected.

P. Fürbringer has communicated observations concerning the value of subcutaneous injections of metallic mercury in syphilis. He declared that this method should only be used when other mercurials are not well borne, and when a rapid mercurial action is not desired.

Dosage.—Hydrarg. depuratum. Mercury is given in ileus, in which it is to act by its mass and weight, in large quantities from 100, 200 to 300 grms., which are to be swallowed in substance. For subcutaneous injection we use 0.05–0.1 per dose, to be repeated once a week.

APPENDIX TO MERCURY.

Since all the other mercurial compounds act exactly like one or the other of the chief preparations of which we have treated, it will be sufficient to speak of them briefly.

The following insoluble compounds act like the mercurous chloride (calomel):

1. Mercurous iodide, hydrargyrum iodatum flavum, HgI. Originally recommended by Ricord in order to produce simultaneously the action of iodine and mercury in scrofulous and syphilitic subjects; practically, however, it is without any advantages (ad. 0.05 per dose ! ad. 0.5 per day).

*2. Mercurous bromide, H. bromatum, Hg. Br.

*3. Mercurous oxide, H. oxidulatum nigrum, Hg_2O.

*4. Mercurous acetate, phosphate, sulphate and nitrate. The officinal are hydrarg. nitric. oxidulatum (ad. 0.015 per dose ! ad. 0.05 per day !) Liquor hydrarg. nitrici oxidulati (ad. 0.1 per dose ! ad. 0.5 per day !)

5. Mercuric sulphide, HgS. and its compounds, such as hydrarg. sulphuratum nigrum, s. æthiops mineralis and the H. sulphuratum rubrum s. cinnaboris—cinnabar.

The following compounds act like mercuric chloride (corrosive sublimate):

1. Mercuric iodide, H. biniodatum rubrum, HgI_2., soluble in tartaric acid but not in water (ad. 0.03 per dose ! ad. 0.1 per day !)

*2. Mercuric bromide, $HgBr._2$, with difficult soluble in water.

3. Mercurial oxide, hydrargyrum oxidatum Hg.O. under two forms. H. oxidatum s. præcipitatum rubrum (ad. 0.03 per dose ! ad. 0.1 per day !) and H. oxidatum via humida paratum, slightly soluble in water, but quite soluble in acids. It is especially used in diseases of the eyes, as blepharitis ciliaris chronica, when there is considerable swelling and thickening of the edge of the lid, to be applied once a day before bedtime in the form of an ointment.

a. Unguentum hydrargyri rubrum—1 part of HgO and 9 parts of lard.

b. Unguentum ophthalmicum, 1 part of HgO to 30 parts of ol. amygdal. and 19 parts of cera flava.

c. Ung. ophthalmic. compositum, 1 part of HgO to 12½ parts of constituens (adeps, cera flava, camphora, ol. amygdalorum, zincum oxydatum).

*4. Mercuric salts.

5. Mercur-ammonium chloride, H. amidato-bichloratum, s. precipitatum album, $HgCl+HgNH_2$. It is used in diseases of the eyes like the mercuric oxide. It is also used in diseases of the skin depending on the presence of pediculi (pithyriasis versicolor, herpes circinnatus and tinea after the separation of the hair. Also used for crab-lice.

Unguentum hydrargyri præcipitati albi, 1 part to 9 parts of lard.

Treatment of Mercurial Poisoning.—Acute poisoning is generally produced by the corrosive sublimate, but the treatment is the same, even if the poisoning has been caused by the analogous preparations. If vomiting does not occur spontaneously, it must be produced immediately either by a mechanical irritation of the pharynx or by the subcutaneous injection of apomorphia. Then milk and albumen are administered in order to diminish the local effect upon the walls of the stomach. As an antidote we may administer the freshly prepared hydrated sulphide of iron (prepared by adding alkaline sulphides to a solution of ferric sulphate) or a paste of iron powder mixed with flowers of sulphur. The treatment of the acute gastro-enteritis is the ordinary one.

THE METALLOIDS.

ARSENIC, PHOSPHORUS, ANTIMONY, BISMUTH, AND NITROGEN.

The members of this group of elements, of which vanadium, which is not used therapeutically, and nitrogen form a part, are chemically analogous ; of these substances, antimony and bismuth form the connecting link between the metals and non metals. There is a marked similarity in the effect produced by the individual members of this group upon the organs and functions of the body. This, according to Binz, is owing to the fact that the oxides of arsenic, antimony, bismuth, vanadium, and nitrogen, and also yellow phosphorus produce an extraordinarily strong oxidation in those tissue cells, which are capable of putting in violent action atoms of oxygen that are held in very loose combination. The elements, arsenic, antimony, bismuth, etc., are therefore without any direct action upon the body, being only the indifferent carriers of the exceedingly active atom of oxygen. While therefore all of the

soluble preparations of arsenic, antimony, bismuth, and vanadium, have a poisonous influence upon the organism, the acids of phosphorus have a much less poisonous effect because in these the oxygen is held in firmer union than it is in the arsenious acid, etc.

Most of these combinations do not form albuminates with the albuminous substances. In this respect they differ from the metals. They have a paralyzing effect upon the central nervous system.

Most of the internal organs undergo a fatty degeneration under the influence of these substances. The glycogen disappears from the liver.

Upon the bones phosphorus and arsenic have been shown to exert a similar influence as far as concerns the formation of osteogenic tissues.

The compounds of phosphorus, arsenic, and antimony with hydrogen have an effect similar to that of sulphuretted hydrogen, being especially powerful agents in causing reduction of the blood.

ARSENIC—ARSENICUM.

Arsenic is the connecting link between the metals, the physical properties of which it possesses (lustre, specific weight, etc.), and the metalloids. On the one hand it is allied to antimony and bismuth, on the other to phosphorus and nitrogen. In its chemical relations it bears the greatest resemblance to phosphorus, so that phosphorus, antimony, and arsenic form a triad of elements.

It occurs in nature partly pure (with cobalt) or in combination with sulphur (auripigment, realgar), metals (iron, copper, nickel arsenites) and with oxygen (arsenious acid anhydride) or in the form of the salts of arsenious acid (flowers of cobalt.)

Like phosphorus, it is dimorphous and can be obtained either as a black, shining mass (amorphous arsenic), or of a steel gray color and having a metallic lustre (crystalline arsenic). In moist air both forms undergo oxidation, the first however with more difficulty. When heated in oxygen it is converted into arsenious acid anhydride.

Pure metallic arsenic, and its pure sulphur compounds, are, as such, entirely harmless. But the many impurities of the various acids of arsenic, or its conversion into such in the presence of moisture, give it its poisonous properties (C. Schmidt.)

For this reason, and because the acids of arsenic only are used therapeutically we shall consider only these, together with the potassium salts, the latter being even more poisonous than the former because of their greater solubility. Arsenic acid has an effect exactly similar to that of the arsenious acid, only somewhat weaker (Marmé.)—The same may be said of the organic arsenates, the combinations of arsenic with the alcohol radical, such as the dimethyl oxide of arsenic (kakodyloxide) $As_2(CH_3)O_4$ and the dimethyl-arsenic acid (kakodylacid) As $(CH_3)_2OOH$; also the diphenyl arsenic acid (phenylkakodyl acid) (C_6H_5) AsO.OH (Lebahn and Schulz).

Arsenuretted hydrogen produces in part similar symptoms to those resulting from arsenious acid (severe abdominal pains, vomiting, and great muscular weakness), but on account of its greater diffusibility these are more violent, and come on more rapidly; it also produces hæmoglobinuria.

I. ARSENIOUS ACID.

Arsenious acid, As O_3H_3 is only known in combination with metals, and can not be isolated. Arsenious acid anhydride (arsenic trioxide) (As_2O_3= O As—O—AsO) however occurs in nature as flowers of arsenic, and can be prepared artificially by burning arsenic in oxygen.

Arsenious acid anhydride is also dimorphous, and both forms are with difficulty soluble in water.

Opaque, crystalline arsenious acid is soluble in 500–1000 parts of cold water, and in 400 parts of boiling water, while the amorphous, glassy, transparent form of the acid into which the first can be changed only by long-continued boiling, is soluble in 10 parts of boiling water. The solution has a slightly acid reaction and metallic taste.

The solutio potassii arsenicosi (Sol. Fowleri) is prepared by taking 1 part each of arsenious acid, pure potassium carbonate, and distilled water, mixing and boiling these until the solution has become clear, then sufficient distilled water is carefully added until the solution is of the strength of 1 part of arsenious acid to 90 parts of the solution.

PHYSIOLOGICAL ACTION.

This ancient and well known poison, which was the only poisonous component of the famous aqua Toffana, has openly or secretly been the death of an incalculable number of people. Inasmuch as it is used in many of the arts, and manufactured every where, it is easily obtained. In spite of its frequent use, however, its action upon the organism has only in recent times been subjected to careful investigations; these have not been able to explain satisfactorily the many contradictions in the study of arsenical poisoning.

Disposition of Arsenious Acid in the Organism.—Arsenious acid when brought in contact, in solution, with the broken skin, ulcers of the skin, or any of the mucous membranes, is absorbed into the circulation. It is more readily absorbed by the empty stomach than when the viscus is full. Its presence can be shown in the blood corpuscles (not in the serum), in all of the organs and in the bones. It is excreted by the bile, but chiefly by the urine, and it is also said to have been found in the sweat. Elimination has begun even during the first 5 hours of the poisoning, and if life be spared, it is usually completed after 2 or 3 days, so that often no trace of arsenic is found in the bodies of those who have died a long time after the administration of the arsenic, which was the cause of death (Grohe.)

Only few cases are on record in which traces of arsenic have been found in the body a considerable time after the poisoning (10-20 days).

General Symptoms of Arsenical Poisoning.—Since the toxic effect of arsenious acid upon animals is the same as upon men, we shall in the following account avail ourselves only of the better and more frequently observed symptoms of arsenical poisoning in men.

The single or not often repeated administration of small doses (0.001–0.005 grms.), gives rise to rather vague symptoms, varying in different individuals, and with difficulty recognizable or appreciable. There is a feeling of warmth in the œsophagus and stomach and appetite is increased so that there is a feeling of hunger.

The various functions are more energetically performed; among these are those of the heart and brain, the respiration, temperature aud those of the genital and excretory organs. But even if these small doses are continued for a long time, serious symptoms of poisoning set in. There is a feeling of constriction in the throat, dryness of the mucous membranes and throat, pain in the region of the stomach, nausea, vomiting and purging; there is also fever, accompanied by headache and sleeplessness. When the drug is suspended the health may be entirely restored.

Acute Poisoning with Danger to Life.—This can be produced in adults by doses of 0.01 grms.; 0.1 grms. is the smallest dose, however, which can be considered fatal, death resulting in a few hours, days, or at most two weeks. The symptoms vary with the size of the dose, being sometimes chiefly referable to the brain and spinal cord, at other times to the digestive canal.

Immediately after swallowing the sharp-tasting poison the patient is seized by the feeling of constriction in the throat, and a few hours later by terrible pains in the abdomen, nausea and severe vomiting and diarrhœa. The latter symptoms may be almost choleriform, rice-water and sometimes even bloody stools, cramps in the calves of the leg and aphonia setting in. The face becomes deadly pale, the pulse very weak and irregular; there is also present a feeling of anxiety, due to great difficulty in breathing; general cyanosis then sets in, followed by loss of consciousness, delirium, convulsions and death.

When very large doses are given, the gastric symptoms are often entirely absent, and death sets in with the presence of cerebral symptoms, of sudden collapse, or epileptiform convulsions as from narcotic poisons.

The quantity of urine is generally diminished and contains albumen and blood.

When acute or sub-acute poisoning does not end in death it often results in sequelæ which last for a long time; such as loss of appetite, gastro-intestinal catarrh, and in consequence of this, wasting; we have also cutaneous sores, gangrene of the skin and neuralgias. After single, very large, but not necessarily fatal doses, paralyses are often observed to follow, but the region affected varies in different patients. The extensors are more frequently affected than the flexors. The paralyzed muscles undergo atrophy, but can be much improved by rational treatment (electricity).

Single large doses which are not fatal, or the long-continued use of small quantities, either medicinally or through unavoidable circumstances, leads to chronic poisoning.

Such unavoidable introduction of arsenic is caused in workmen employed at or with manufactures or arts in which arsenic is used (arsenic colors, paris green, wall paper, etc.) The symptoms of chronic poisoning are very various. When the patient lives in an atmosphere tainted with arsenic dust, there are eczematous inflammations of the skin, inflammations of the eyes, in addition to the general digestive disturbances depending partly upon a chronic arsenical gastro-intestinal catarrh and partly upon the general effects of the poison. The skin is pale, and the whole body exceedingly anæmic. Frequently there is constant headache and psychical depression, the hair and nails fall out, ulcers form upon the skin, mucous membrane of the nose and external auditory passages, there is a severe inflammation of the larynx with an annoying cough. In this *form of poisoning* also we often have sensory and motor pareses.

The cause of death is often consumption of the lungs (tabes arsenicalis) and dropsy.

Effect of Arsenious Acid upon the Individual Tissues and Organs.—The fact that arsenic exerts an escharotic action, especially upon the skin and mucous membranes, particularly those of the gastro-intestinal canal, as well as the generally received fact that the bodies of those who have died from arsenical poisoning do not decay, but dry up and become mummified, has led to the opinion that arsenious acid, like many other metallic poisons, enters into chemical combination with the organic substrata, that is to say, with the albuminoid bodies. Upon this alteration of the albuminous molecules depends the destructive escharotic and antiseptic action of the drug. Liebig expressed the opinion that under its influence the albumen is decomposed and sulphuretted hydrogen formed.

Direct experiments, however, have not yet shown that arsenious acid changes the albuminates of the blood in any noticeable manner (Kendall and Edwards, Herapath). It has been further shown that arsenious acid is absolutely without any influence upon the decomposition of albuminoid bodies, as for instance the ferments of the gastric juice ; here the acid does not chemically combine either with the albumen or the newly formed pepsin ; nor does it alter the reaction of these fluids, or lose any of its own properties (Schaeffer and Boehm). As to its effect upon the process of decomposition and the ferments, our observations vary. According to some, arsenious acid when directly applied to ferments, does influence their fermenting power (Buchheim and Savitsch). Indeed, it is supposed that yeast fermentation is quickened by its presence in that it aids in the development of bacteria.

The mold fungus is also said to grow better under its use. But it seems to interfere with the development of the urine and milk ferment (Boehm and Johannsohn). The decomposition of the muscles, blood and nerves is hindered by medium quantities. There is not, therefore, even a single positive reason for the belief that arsenious acid enters into a chemical combination with the organic substrata, although such a supposition would very well explain a large number of the effects of the drug.

Buchheim–Savitsch therefore think that the poisonous effect of arsenious acid is not due either to the arsenic acid or to itself as such (they believe arsenious acid analogous to phosphoric acid in this respect) although they are unable to explain to what new form of the substance this effect is due. The fact that the

arsenious acid as such is to be found again in the urine, is also against this theory.

The latest observations of Binz and Schulz have shown that in some dead as well as living tissues (intestine, liver, brain, etc.) the protoplasm has the power of setting in motion the oxygen which is in combination with the arsenious acid. Arsenious acid is thus converted into arsenic acid and *vice versâ*.

From this fact they conclude that the constant change which these acids undergo, the constant oxidation and reduction which takes place in the albuminous molecule in which they are contained, causes an unceasing movement of the oxygen atoms, and thus produces the poisonous or therapeutic effect. According to Binz arsenic is only the carrier of the active oxygen molecule, just as the nitrogen is in the actively irritating nitrous oxide (NO), and the caustic nitrous acid (NO_2) ; here the nitrogen is without any direct effect. Not all of the protoplasmic cells are able to reduce or oxidize arsenic ; only those portions of the body, therefore, are affected by arsenic, the cells of which have this power (predilection places, Binz). All of the effects of arsenic, and especially those which cannot be otherwise explained are explicable by this theory.

Skin.—The unbroken skin is unaffected by arsenical paste. But ulcerated portions of the skin, as well as those affected by lupus are thus entirely destroyed ; when a portion of the latter is covered by arsenical paste, it appears in 3–5 days as though numerous pieces had been hacked out of it, but between the small openings are little islets of healthy skin which have remained unaffected ; from these healthy portions cicatrization rapidly takes place (Kaposi). In the actively growing protoplasm of the lupoid tissue, the conditions necessary for the active interchange of the oxygen, are present, while in the hard connective tissue of the healthy skin, these conditions are wanting (Binz).

Mucous Membranes.—Hebra's paste has a similar effect upon the mucous membrane of the anterior portion of the nasal cavity. Here also only the lupous portions are affected, while the healthy mucous membrane remains unaffected (Rossbach).

The action upon the mucous membrane of the digestive canal, however, is very intense. Even in the lesser degrees of poisoning, there is extensive hyperæmia and ecchymosis, here and there also erosions. But a real caustic effect does not occur, even in the severest cases, unless large quantities of the arsenic lie directly upon the mucous membrane. Generally the glands of the stomach and intestine are affected ; (adenitis

parenchymatosa—glandular gastritis—Virchow and Wyss); that is to say, those tissues in which the greatest amount of metamorphosis takes place, so that again Binz's theory is confirmed.

Intestine.—Arsenic first increases the peristaltic movements of the intestine; thus the whole of the intestinal canal falls into a more or less equable tonic contraction. The visible portions of the intestine become very pale, appearing almost pure white (Lesser).

In the tissues of most of the abdominal and other organs arsenious acid like phosphorus produces a fatty degeneration, probably in consequence of the increased decomposition of the albuminoid bodies. Saikowski gave to rabbits 0.02 grm. of arsenic acid for 2 or 3 days and found that the liver became very much enlarged and in the middle of each acinus he found the cells filled with globules of fat, more numerous indeed than in phosphorus poisoning. The liver fat however was, contrary to the usual rule, not pigmented. The urinary tubules of the kidneys were full of fat globules, and the little epithelium that still remained had also undergone a fatty degeneration; the epithelium of the gastric follicles was also fatty, and the follicles filled with fat. The muscular tissue of the heart and diaphragm was also undergoing fatty degeneration. Grohe found the same appearances in a two year old child after the poison had been continued for two days.

There is also a diminution or an entire disappearance of the glycogen in the liver, and in the latter case of the sugar also. This disappearance of glycogen often precedes fatty degeneration. Puncture of the 4th ventricle does not so readily cause diabetes in animals poisoned by arsenic (although the urine still reacts to Trommer's test). Curare will not cause diabetes in animals under the influence of arsenic (Saikowski). Sugar injected into the blood of these animals appears in the urine as such, but notwithstanding this no glycogen can be found in the liver and muscles (Luchsinger). Long continued arsenical poisoning produces atrophy of the liver.

Bones.—Very small doses of arsenic produce considerable changes in young, that is not full grown, animals. The growth of bone, both from the epiphysis and periosteum is very much increased. The bone becomes longer and thicker; the spongy bone tissue (cancellous) is changed into compact and solid tissue; the carpus and tarsus, for instance, were found entirely composed of compact tissue. The bone corpuscles of the compact layers become smaller and more numerous. Even the

Haversian canals cover a less area and are less numerous (Maas, Gies).

Nervous System.—In frogs there is, at first, a slight increase of irritability (Lesser) followed very rapidly by paralysis of the gray substance of the spinal cord. On the other hand, the irritability of the motor nerves and muscles is longer maintained although it also is considerably weakened (Sklarek and A. Lesser).

First the nerve centers, then the peripheral nerves and finally the muscles are affected.

Even in warm-blooded animals and men there are frequently paralytic symptoms on the part of the brain and spinal cord, (page 228). Scolosuboff, in fact, found in cases of chronic and acute poisoning 30 times more arsenic in the brain and medulla oblongata than in the liver and muscles.

Respiration in warm-blooded animals.—At first the number and depth of the respirations increase in consequence of a direct irritation of the respiratory centers and of the vagus terminal filaments in the lungs. Later on, however, the respiration becomes weaker and slower in consequence of a paresis of the respiratory center. Finally, when the respiratory muscles of the chest and abdomen scarcely act at all, the muscles of the face have an increased action, the alæ nasi and the mouth opening with each respiration. The larger the dose of the arsenic the more rapidly this second stage of its action sets in. The respiratory disturbances are independent of the condition of the circulatory apparatus (Lesser).

Circulation.—The heart of the frog, soon after the poisoning, begins to beat more slowly and feebly, later on it becomes irregular. Finally the heart stops entirely in diastole, but in such a manner that for a half hour afterward electric irritation will cause a contraction (Lesser). Even after the heart has stopped beating, the frogs continue to live for about 10 minutes.

In warm-blooded animals, small doses injected into the blood, increase the rapidity of the pulse, but do not raise the blood pressure (Lesser). Medium doses produce an increase and then a decrease, while large doses are followed by an immediate decrease in the number of the heart's beats. The increase in the pulse is due to a depression in the vagus tonus and increased irritability of the ganglia of the heart. The diminished pulse is dependent upon a depression of these ganglia.

The force of the heart's beat gradually becomes weaker and weaker without any antecedent period of increased strength. The muscle of the heart itself is certainly not paralyzed by ar-

senic, but frequently retains its irritability for an uncommonly long time; this is especially true of the auricles, which were found pulsating 17 and even 26 hours after death (Kunze, Lesser). The vaso-motor center, the vasor nerves and muscles are unaffected by arsenic. Bœhm believes that there is a paresis of the peritoneal vessels, but Lesser says positively that the vessels of the mesentery and peritoneal layer of the intestine are even narrower, and contain less blood; their tension depending upon the condition of the heart.

Large doses lower the temperature cf the body considerably (from 1–5° C.); more so during the first than the second stage of the action of the drug. The size of the dose has relatively but little influence upon the rapidity and amount of decrease of temperature (Lesser).

Influence of Arsenic upon Nutrition and Interchange of Materials in the Body.—According to the most recent observations, very small doses seem to exert a very favorable influence upon growth and nutrition (compare page 234). The animals experimented upon by Gies grew heavier and fatter under the use of such doses. At the same time, however, there was also fatty degeneration of the heart, liver and kidneys. The favorable influence upon the growth of the bones, we have already spoken of. These small, harmless doses have not the least influence upon the decomposition of albumen and excretion of nitrogen (v. Boeck).

The matter is entirely different, however, under the use of large doses. The experiments of C. Schmidt and Stuerzwage as well as those of Lolliot, according to which the use of arsenic is followed by a diminution in the amount of nitrogen excreted are entirely untrustworthy. The former because the poisoned dogs vomited all their food or ate nothing at all, so that the diminished amount of nitrogen excreted might depend upon the want of food; the latter, because neither the quantity of nitrogen taken in with the food, nor the amount excreted with the urine had been determined, while the conclusions were based entirely upon the percentage of nitrogen contained in the urine, calculations which are entirely untrustworthy. Gæthgens, Kossel and Berg observed in the most exact manner the effects of toxic doses of sodium arsenite upon a starving dog, and one of equal weight fed upon nitrogenous diet. They found an increased excretion of nitrogen, that is to say, increased decomposition of albuminoids in the tissue cells. This increase in the decomposition of the albuminoids occurred, according to Gæthgens, *without* any correspoding elevation of temperature.

Concerning the Tolerance for Arsenic.—We have seen that not only large but even the smallest, scarcely perceptible doses of arsenic (arsenious acid) produce severe symptoms of poisoning, either acute or chronic, and sometimes death. In the face of this fact, the assertion of Schallgruber and later on those of Tschudi and others, that men as well as animals could become accustomed to taking arsenic, so as to be able to take with impunity doses two or three times as large as those that are ordinarily fatal, and that such animals become stronger, healthier and fatter under the use of arsenic, could scarcely be believed. In the former edition we were very guarded about expressing an opinion concerning this point, because there did not appear to us to be positive observations concerning the possibility of such tolerance, while on the other hand chronic arsenic poisoning was a well known condition. In the intervening time, however, Gies has made observations upon animals with reference to this point, with the following result:

1. Ill-nourished and ill-kept animals (rabbits) cannot endure even the smallest daily doses of arsenic (0.0005–0.002 daily). They become more and more depressed from day to day, do not eat, have diarrhœa, an ugly hide, and die almost reduced to skeletons in the course of three and a half weeks. *Post mortem* we find gastric catarrh with hypertrophy of the mucous membrane, fatty liver, and other signs of chronic arsenical poisoning. Gies believes that the ill-nourished condition of the animals has not enabled them to withstand the poisonous effects of the drug.

2. Young, strong and well kept animals (rabbits, pigs and cocks) not only bear small doses (0.0005–0.002) very well, but, in comparison with animals not fed with arsenic, became stronger, growing in every way. The skin or hide became more beautiful and shining, the body became fatter and the bones grew in length and thickness. (Page 231). Even the newly born young of these animals were larger and have stronger bones and a thymus gland of larger size, but were all stillborn; this latter fact Gies explains by the increased difficulty in parturition on account of the abnormal size of the fœtus.

A further remarkable observation which has given rise to many doubts is the fact that animals that were not fed upon arsenic, but which were kept in the same stable with animals *that were so treated*, showed similar changes to those described *above.* This was also the case where the animals were kept in

a cage, in the floor of which holes were bored, and under which arsenic was scattered, although the animals were unable to reach it. Gies explains this by supposing that in the former case volatile arsenic combinations were exhaled from the skin and lungs of the animals that were the subject of experiments or in the latter case from the arsenic underneath the floor of the cage.

3. Full grown rabbits, which had taken 0.0005 of arsenious acid for forty days, were, according to Gies, better nourished, fatter, and presented a thickened layer of bone, due to the arsenic, under the cortex of the diaphyses; epiphyseal growth having already ceased, there was no increase under the epiphysis. It is difficult, however, to reconcile the statement of the excellent health of the animals with the fact that the liver, heart and kidneys had undergone a fatty degeneration.

4. Some animals could not get accustomed to an increase in the dose of the arsenic. As soon as the dose was increased, it was especially noticeable in cocks that the alteration in the osseous system began to become retrograde, while the symptoms of chronic poisoning set in. The animals grew lean, the hair fell out, there was considerable hyperæmia of the stomach and intestines, and severe diarrhœa; also marked fatty degeneration of the heart, liver, kidneys and spleen.

In consideration of the above experiments upon animals (1) and the further fact that sudden death is frequently seen in arsenic eaters (Schaefer in Graz saw thirteen cases in two years), as well as the observation that when even small doses of arsenic have been given for a very long time, symptoms of poisoning have been observed to occur, we cannot maintain that tolerance of even very small doses of arsenic is by any means the rule. The physician must learn to estimate the power of endurance of each individual case. The tolerance of increasing doses of arsenic seems even more doubtful. Those who hold the opposite view can instance the following convincing proofs: 1st. The two Styrian arsenic eaters whom Dr. Kapp presented to the Society of Natural History in Graz, one of whom was a young man of twenty-five years of age, swallowed before the eyes of the auditorium 0.4 grms. of arsenious acid without harm; also Hebra's report of patients suffering from skin diseases, who for several months took daily 0.06, in all 10.0 grms. Again Kaposi's patient, who in the course of twelve months received 22.5 grms. of arsenious acid. Although we are compelled to conclude from these cases that increasing doses of arsenic can indeed be borne for a time without immediate

harm, yet we must not forget that we do not know even in these cases how long this tolerance lasted, nor whether the patients suffered from any sequelæ, such as fatty degeneration of important organs, etc. We still want a series of well-observed cases. The experiments of Gies upon animals, which might be utilized here, are certainly opposed to this view.

THERAPEUTIC APPLICATION.

There are few drugs with which so much fault has been found on the one hand, and upon which so much praise has been bestowed on the other, as upon arsenic. Among its defenders were formerly Harless, Heim, Fowler and Boudin, and recently Isnard. It was always recognized as an active drug, but it was not until the last decennials that the dislike against its use was swept away in Germany by the authority of Romberg, and the application of the drug became general. Experience teaches the following concerning its application :

Arsenic is very much used in malaria (intermittent form). Its utility in this affection has been disputed since the seventeenth century (Wepfer, Helmont and others). Quinine is an almost certain remedy against this affection, and has no disadvantages while arsenic may possibly at least be followed by a toxic effect. Apart from this, however, it is positive that quinine should be preferred to arsenic in all recent cases of intermittent fever. Arsenic may also cure it (this has been proved by the observations of numerous physicians), but not as certainly as quinine. Furthermore, quinine should be used in severe cases of pernicious intermittent fever, where an immediate result is necessary, and where the remedy must be administered in large doses, which cannot be done with arsenic. Under no circumstances can we recommend the constant use of arsenic in this affection, as some individual observers would have us do.

But arsenic will always maintain its place in the treatment of malaria, because under certain circumstances it is of greater benefit than quinine. In the first place, recent individual cases may be observed in which quinine has been useless, while arsenic cures the malady. The circumstances under which this occurs are yet to be formularized by experience. Again arsenic is more useful in inveterate cases of intermittent ; for this purpose it was recommended even by the older observers. *6–10 drops* of Fowler's solution are given 2–3 times daily. *Recently* Isnard has warmly recommended the use of arsenic

in the malarial cachexia, which is so frequent in malarious regions. Although this latter point is not yet decided, yet the drug is certainly worthy of trial in these cases. We do not think that it would be suited as a prophylactic in malarial regions, as has been suggested, although concerning this point more numerous observations are necessary.

Arsenic is a remedy very much used in the various neuroses. Its most recent advocate, Isnard, prescribes it in almost all of the socalled functional neuroses. It has been found of value in some cases of neuralgia. Among the chief of these are those neuralgias which occur periodically, generally in consequence of malarial infection. In recent cases quinine is generally more effective than arsenic, but in old, inveterate cases, according to all experience, our own included, arsenic is preferable. Individual observers (Isnard, for example) have used arsenic from the very beginning of typical cases of neuralgia, and report that they have done so with good effect. But even in the ordinary forms of neuralgia arsenic has been found very valuable, especially in old severe cases affecting any nerve trunk, although the least favorable results are said to follow in sciatica. But we must not expect a uniformly favorable result. Romberg says, that such a favorable result generally follows when the cause of the neuralgia is uterine or ovarian trouble; the more anæmic the patient the more likely will a favorable result follow, while in plethoric individuals an injurious action may appear. Of the many neuroses in which arsenic has been tried, we must mention chorea, in which arsenic is unanimously considered a valuable remedy. Of course it is not used in recent cases, which often recover spontaneously, but only in old and inveterate cases. Sometimes, however, the remedy fails, and we are unable to tell under what circumstances the arsenic may be expected to be effective and when not. The etiology of the trouble (rheumatism—psychical influences) seems to be of no importance as far as the determination of this point is concerned. The drug is well borne by children. Whether arsenic is really as effective in the condition known as "general nervousness" as it is lauded by Isnard, further experience must determine. A. Eulenburg states that he has used arsenic, in the form of subcutaneous injections in the tremors dependent upon disease of central origin (sclerosis disseminata) and found it a very superior remedy.

Should this be confirmed by further experience, it would be a very desirable application of arsenic. Experience must also teach whether it affects only the tremor as a symptom or whether

it exerts an influence upon the central malady; also whether it has any influence upon tremor alcoholicus, saturninus, etc. We have not obtained any very brilliant or satisfactory results, and doubt whether the improvement noted in a few cases (we have seen none in which the tremor was cured) was due to the arsenic or other factors in the treatment (such as rest in the hospital, etc.).

The utility of arsenic in some of the chronic skin diseases, of which psoriasis and eczema are the principal ones, is undoubted. Psoriasis idiopathica is best treated internally by arsenic. Some cases are not cured by arsenic internally alone and in these external treatment should also be inaugurated. The good effects of the arsenic are not noticeable until 14 days of treatment have passed, and weeks go by before the eruption disappears. Even Hebra with his immense experience recognizes the utility of the arsenic in psoriasis, inasmuch as the eruption disappears under its use, but he doubts whether it exerts a really curative effect, inasmuch as it does not prevent the recurrence of the trouble. Although not as certain a remedy for eczema as for psoriasis, arsenic has been found of great value, especiclly in wide-spread universal eczema. The cases should be chronic ones, for if there be any signs of an acute eczematous inflammation, it is apt rather to exacerbate than cure the malady. We can not tell positively in advance in which cases of eczema the arsenic will be successful. On the strength of Salkowski's experiments, Leube made use of arsenic in diabetes mellitus and observed a decrease in the amount of sugar in the urine, together with an improvement in the general health. Several authors confirm this result. The majority (whose ranks our experience leads us to join) have not hitherto seen the slightest benefit result from the use of arsenic in this malady. Kuelz and Fürbringer especially, after careful investigation, are inclined to explain the diminution in the amount of sugar excreted partly by the occurrence of digestive disturbances and partly by the diminished absorption of nutriment.

Leared lately recommended arsenic as the only remedy for certain forms of cardialgia, which occur generally at night in persons of middle age who are subjected to great mental strain. These attacks of cardialgia are unaccompanied by any evident disturbance of the stomach. We have used the remedy in similar cases, with only temporary benefit.

Of the many other conditions in which arsenic has been recommended—Isnard has even given it in tuberculosis and chlorosis—we shall only call attention to its use, in later years, in lym-

phoma maligna (Billroth, Czerny). In some few cases of this kind the remedy was ineffective. But in the other cases, when the remedy was administered internally or injected into the parenchyma of the gland, a decided regression of the new formation and even cure resulted. Winiwarter reported confirmatory observations; there were certainly relapses, but even these gave way when the remedy was reapplied.

Experience has taught us the following general rules for the use of arsenic. It is best borne by anæmic and chlorotic individuals, less so by plethoric subjects. Children bear it very well. But it should be sparingly used in old people, because it easily produces indigestion in these cases. It should not be given when digestive disturbances of any kind, gastric catarrh, etc., exist, nor should it be given during febrile conditions (with the exception of intermittent fever). According to general experience, the best time for its administration is when the stomach is full, that is, after eating. When the remedy is to be continued for some time, there is a difference of opinion as to whether it is best to begin with small doses and increase, or *vice versâ*. At the appearance of the first symptoms of a toxic effect (pressure in the region of the stomach, digestive disturbances, feeling of constriction in the throat, conjunctivitis, etc.) the remedy should be immediately suspended.

Externally arsenic is sometimes used with favorable results in inveterate cases of psoriasis diffusa; here it should be applied in the form of an ointment over the affected portions of the skin. It was formerly much used as a caustic in deeply destructive skin affections, such as epithelial cancer, phagedenic ulcers, lupus, etc. But this method is being more and more replaced, especially in lupus, by scooping out the diseased skin. It can still, however, be used in superficial lupoid ulcerations, which should be dressed for several days with arsenic ointment (1 to 25, Volkmann and Hebra). Arsenic is also much used in dentistry as a caustic, to destroy nerves, laid bare by caries of the teeth.

Dosage and Preparation.—1. Acidum arsenicosum, internally from 0.001 to 0.005 (ad 0.005 pro dosi; ad 0.01 pro die) twice a day in a powder, pill or solution. Fowler's solution, however, should be preferred for internal use.

Externally, used as an Eschorotic.—For painting, wash and dressing (0.1 to 0.3 % solution). As a caustic for dental nerves it should be combined with morphia and creosote.

2. Potassium arsenicosum solutum (solutio Fowleri) acts in proportion exactly like arsenious acid (contains one part of arsenious acid to 90 parts of the solution). It is almost the only preparation used therapeutically.

From 0.05 to 0.2 two or three times daily (ad 0.3 pro dosi; ad 1.0 pro

die !), either pure or mixed with water (1 to 3 of distilled water), best given a short time, one-fourth to one-half hour after meals. In children 0.01 to 0.03 pro dosi diluted and not pure.

For subcutaneous injection in tremor Eulenberg uses a mixture of 1 to 2 of aq. dest. and generally injects 20 to 30 markings of Pravaz' syringe, that is to say about 0.15 to 0.2 of p. a. s., and yet he says he has never seen any serious results follow.

3. Pulvis arsenicalis cosmi—cosmic powder—consists of 120 parts of hydrarg. sulphuratum rubrum, 8 parts of carbo animalis, 12 parts of resina draconis and 40 parts of acidum arsenicosum. This powder is mixed to a paste with water, then laid on to a thickness of two or three millimetres and then covered with charpie. This is an escharotic which causes great pain.

4. *Hebra's Paste.*—Acid arsen. 0.5; cinnab. fact, 2.0, ung. rosat., 15.0.

TREATMENT OF ACUTE ARSENICAL POISONING.

Until an antidote is obtained the most important thing to do is to give an emetic or use the stomach pump. Then a preparation is administered which is to render the arsenious acid inoperative. The best is the officinal antidote of arsenic, already described under the head of iron preparations. This is a mixture of iron and magnesia. Concerning its action and administration we refer to page 187. In the absence of an emetic or stomach pump we should endeavor to excite vomiting by mechanical irritation of the pharynx, administer milk and other mucilaginous drinks. Later on the bowels should also be emptied by a purge or clysma.

The further treatment of the collapse, gastro-enteritis, etc., is to be conducted according to general therapeutic rules.

PHOSPHORUS.

Of this substance, which in its chemical properties resembles sulphur, there are two modifications: 1. The officinal or ordinary phosphorus, which is exceedingly poisonous. 2. The red or amorphous phosphorus, which is obtained by long continued heating of the previous preparation in an indifferent atmosphere.

Ordinary phosphorus is a yellowish white, semi-transparent body, which is soft as wax at ordinary temperatures and becomes very brittle in the cold. In the air it exhales a vapor that shines in the dark, has a garlicky odor, and burns at 60°. It is only very slightly soluble in water, much more so in alcohol, ether and ethereal and fixed oils; most soluble in the bisulphide of carbon.

Amorphous phosphorus is insoluble, even in the carbon bisulphide, and burns at 260°.

PHYSIOLOGICAL ACTION.

Phosphorus has a varying effect upon the organism according to the size of the dose and the length of time that it is used. In larger doses it is a very severe irritant for certain tissues, especially the specific parenchymatous elements of the liver, kidneys, stomach and muscular system, so that in a short time *these undergo* a fatty degeneration and necrobiosis. (Vir-

chow.) Very small quantities given for a long time do not affect the above mentioned tissues, but act as strong irritants to entirely different varieties of tissue, especially the ostiogenetic substances and the interstitial tissue of the stomach and liver. This irritation does not lead to degeneration, but to hypertrophy of the affected tissues, resulting in permanent new formations. (Wegner). Aufrecht asserts that as far as the liver is concerned, large doses of phosphorus may produce parenchymatous as well as interstitial connective tissue disease.

We shall discuss with considerable minuteness the formative action of very small doses of phosphorus as studied by Wegner, because therapeutically this is of greater interest.

Action of the Phosphorus upon the Organism.—Formerly it was supposed that phosphorus could not be absorbed as such, because it was only with difficulty soluble in water. It was therefore supposed that the real cause of the poisonous effect of phosphorus upon the body was its conversion into phosphoreted hydrogen (Hoppe-Seyler and Dybkowsky), or its oxidation into phosphorous and phosphoric acid. But it is now known that at least 0.000227 parts of phosphorus are dissolved in 100 parts of warm water, and that even larger amounts can be dissolved in the intestinal fats and bile (0.01 to 0.026 to 100). (Husemann, Buchheim, Hartmann.) In this way phosphorus can be absorbed. Phosphorus has also been found as such in the blood, tissues and excretions. (Dybkowsky.) The characteristic poisonous effects of phosphorus can be produced by injecting phosphorus as such into the blood. We may therefore consider that the chief portion of the effect upon the organism is produced by phosphorus under its own form, and only to a slight extent by its products of oxidation, namely, phosphoric and phosphorous acids, especially since the latter, even when directly injected into the blood in much larger quantities than if formed from the phosphorus, are without effect. Nor can the phosphorus action be due to the phosphoreted hydrogen, for this can only be formed in the intestines, while phosphorus produces its effect when injected directly into the blood.

The finer processes of the chemico-physiological action of phosphorus are still unknown. Binz explains the toxic effects which it produces in the tissues (paralysis, fatty degeneration of cells and increased excretion of urea), effects which are in the minutest particulars similar to those produced by arsenic, *in the same manner* as he does the action of arsenic.

"Phosphorus produces in the easily oxidizable cells of the body, which it reaches dissolved in fat, active oxygen, just as it does when in contact with water and air, and this is the active agent. Its poisonous properties are lost when it is changed to red phosphorus, which is with difficulty oxidizable, or when its introduction into the stomach is immediately followed by ozonized oil of turpentine, which immediately oxidizes it to the acids of phosphorus, which are no longer able to produce active oxygen. Phosphorus produces active oxygen very rapidly, so that its destructive action is rapid and severe. Arsenic is not so rapid and is less energetic, but this is compensated by the duration and recurrence of the effect in the case of the latter." We can certainly not explain the poisonous action of phosphorus by its oxidation by means of oxygen withdrawn from the blood globules. Hermann has shown that 0.1 grm. of phosphorus would require only 0.13 grm. of oxygen to be converted into phosphoric acid. The loss of this amount of oxygen is certainly too small to explain the death of an adult man.

Phosphorus is excreted in the urine either unchanged or under the form of phosphoric acid (Falck junior.). Phosphorous acid has not been found in the urine.

ACTION OF VERY SMALL, LONG-CONTINUED DOSES OF PHOSPHORUS.

Osseous System.—Wegner experimented on rabbits, dogs, cats and fowls with doses of phosphorus so small that they produced no disturbance of the stomach or liver. He found after long continued use of these that noteworthy alterations were produced in the bones. The daily dose of finely divided phosphorus for a half-grown rabbit was 0.0015 grm. Full-grown rabbits and young fowls received double this quantity (0.003 grms.). Full-grown fowls took even larger quantities without any difficulty. Dogs and cats, however, were more susceptible to the action of phosphorus. In the course of experiments continued for months, Wegner was able to double the original dose of phosphorus, inasmuch as the animals readily became accustomed to the poison.

The alterations occurring in consequence of this phosphorus diet were most easily to be seen in growing animals. The bones of these animals are somewhat different from those of full grown animals.

In situations in which normally the cartilage develops into

cellous tissue, that spongy, bony tissue which contains much red marrow, we find, under the influence of phosphorus, a bony tissue formed which is firm and hard, like the compact tissue found on the outside of the long bones. The cancellous tissue which was already formed before the beginning of the administration of the phosphorus remains entirely unchanged.

The substance of the bone formed under the influence of phosphorus appears microscopically as well formed bone; the large marrow spaces are contracted to the ordinary width of the Haversian canal in the compact bone tissue, the larger part of the proliferated cartilage cells being converted not into marrow cells, but into bone corpuscles, which have around them the usual amount of intercellular substances.

If the phosphorus is continued, the intermediate cartilage in the long bone gives rise to the formation of these compact masses of bone, while the spongy substance which was formed before the administration of cartilage, is gradually wasted away to give place to the medullary cavity, which is thus physiologically formed. After a certain time all of the cancellous structure at the end of the diaphysis has been replaced by compact bone tissue.

If the use of phosphorus be still continued, even the hardened bone tissue formed under its influence, that is the old layers, becomes rarified and wastes away, being turned into red marrow just as the normal cancellous tissue had been, to give place to the medullary cavity.

Even that portion of the bone which is contiguous to the periosteum, and which is developed from the periosteum, is also altered in a similar manner, but here the alterations are only recognizable by the aid of the microscope; the Haversian canals are seen to become smaller, but never entirely occluded.

In addition to these alterations, Wegner thought that animals fed on phosphorus increased in size and strength; the osseous as well as the muscular system undergoing a considerable increase in strength. The bony shell became thicker at the expense of the medullary cavity.

Even in full grown animals, phosphorus caused a condensation of the cancellous tissue. In fowls especially this advanced to complete occlusion of the original medullary cavity by real bone tissue, so that the bones were no longer tubular but solid pillars.

If in growing animals the administration of phosphorus be suspended from time to time, we will find that the cartilagi-

nous ossification has taken place in layers of compact tissue alternating with the ordinary cancellous tissue.

The composition of the bone tissue of animals thus fed on phosphorus is in no way different from that of normal bone, either as far as the percentage of inorganic and organic ingredients is concerned, or in any increase of phosphatic salts.

Wegner found further, that only phosphorus itself, and not any of its derivatives, had this influence upon the osseous system, in consequence of exerting a specific formative irritation upon the osteogenic tissues.

That this great production of bone tissue is not due to an increase in the percentage of phosphates in the blood during the time that phosphorus is given in the diet, was shown by Wegner on animals which he fed on a diet void of phosphates during the time that they received phosphorus; the result was that in these animals the epiphyses of the bones showed the same abnormal, dense bone substance, with this difference, however, that it was not real hard bone tissue, but only an osteoid tissue (just such as is found in rachitic human bones).

Up to the present time, only a single series of experiments has been made by Wegner himself, as to whether human bones react in the same manner to phosphorus as those of other animals. The results obtained seem to show that they do.

The direct local effect of phosphorus fumes in moderate concentration, upon the periosteum, is to produce a periostitis; if the vapor be very concentrated this may be accompanied by suppuration. It leads to the necrosis, so frequent in those working in match factories, of the maxillary bones, the inferior maxillary being more commonly affected. This process begins in carious teeth, and is therefore to be considered as a direct effect of the phosphorus.

Action of Medium Doses of Phosphorus, Which have been Continued for a Long Time upon the Digestive Canal, Liver and Organs of Respiration.—We have already stated, that apart from the effect upon the bones, small doses of phosphorus produce no other disturbance as far as can be observed. The animals remain well nourished, and show no signs of any functional or anatomical change. When however the dose is increased slowly (whether administered internally or inhaled), so that no acute or sub-acute poisoning takes place, we find that the interstitial connective tissue of the liver and stomach is irritated. Chronic indurative gastritis is developed, accompanied by hyperæmia, hæmorrhagic infarctions, and extraordinary hypertrophy of the gastric mucous membrane, due to an

abnormal development of the interstitial connective tissue, which, in health, can scarcely be demonstrated. We also have chronic hepatitis with icterus and atrophy of the liver substance ; the final result is a smooth or lobular or granular atrophy of the liver (the so-called cirrhosis). These facts were determined by Wegner, through experiments upon animals. Similar results were obtained by observation of workmen in match factories.

The inhalation of the vapors of phosphorus readily produces in men as well as in animals a bronchitis. In men it may even produce pleuro-pneumonia.

Acute and Subacute Phosphorus Poisoning, brought about by the Administration of large doses of Phosphorus.—Phosphorus (in the shape of phosphorous matches) is frequently used for suicidal purposes.

The smallest fatal dose is as low as 0.05. grms. for adults ; while a few milligrams taken finely subdivided may be fatal to children. Large pieces may pass through the whole length of the intestinal canal, almost harmlessly and without being dissolved, to be passed off with the fæces.

The symptoms of poisoning begin several hours after the administration of phosphorus. Death only occurs after several days or even weeks.

The local effects which result from the swallowing of phosphorus are not very severe, and consist of gastric catarrh and superficial ulcers in places with which the phosphorus has lain in contact for some length of time. The way in which these alterations are produced is not known. Schultzen and Riess, as well as Hermann, believe that it can not be due to any escharotic action, since phosphorus applied subcutaneously in substance is entirely harmless, while solutions of albumen are not altered by phosphorus. Munk and Leyden believe that the local effect depends upon the oxidation products of the phosphorus, which in their nascent state withdraw water from the tissues and thus destroy them. Binz's explanation we have already referred to, (page 230). The results of these local effects are pain in the stomach, nausea and vomiting of dark, shining and sometimes bloody masses, leaving a garlicky odor.

The effect of these doses of phosphorus upon the general system is due mostly to fatty degeneration of a large number of organs.

It is not observed until a period of apparent recovery has followed the local manifestations.

These affections are again ushered in by gastric pain, vomiting and diarrhœa. *Post-mortem* examination reveals swelling of the gastric mucous membrane, and especially also of the duodenum (Munk and Leyden), fatty degeneration of the glandular cells of the stomach (Virchow), or according to Ebstein, only of the cells of the mucous, and not of the gastric follicles. There is also fatty degeneration of the gastro-intestinal muscular layer.

Soon considerable hypertrophy of the liver sets in, accompanied by icterus, in consequence of fatty degeneration of the liver (v. Hauff), and occlusion of the finest biliary ducts by their enlarged epithelial cells which have undergone fatty degeneration. According to Aufrecht, the phosphorus first sets in motion a series of chemical processes in the liver cells, which lead to the formation of albuminoid granules and fat globules within the protoplasm of the liver cell, but do not necessarily result in their destruction; for if the dose has not been too large and life is maintained, a complete return of the liver cells to their normal condition and function results. When the administration of phosphorus, however, is frequently repeated, the liver cells are no longer able to get rid of the albuminoid granules and fat globules. The cells then begin to take on a pale shining appearance, with well marked granules within them.

Apart from this, the frequent administration of these doses of phosphorus leads to an affection of the interstitial connective tissue. In the livers of young rabbits the glycogen disappears in 1½ days after the giving of 0.02–0.03 of phosphorus.

In consequence of the fatty degeneration of the muscular fibers of the heart, after a slight increase in its action, its beat becomes weaker and weaker, while the frequency is variable. The sounds of the heart, especially the first, are scarcely audible. This fatty degeneration also attacks the muscles of the extremities, so that great weakness and even paralysis set in.

At the same time hæmorrhages from all of the mucous membranes occur—from that of the nose, intestinal tract, and uterus. Severe menorrhagia and metrorrhagia, which are checked with difficulty, occur. Hæmorrhages take place even into the subcutaneons connective tissue. All of these are due to the fatty degeneration affecting the walls of even the finest vessels, (Wegner), and also to the uncoagulable condition of the blood, *which does not* coagulate even 20 hours after death. (*Schuchart*).

The temperature varies with the severity of the poisoning. In the beginning it is sometimes elevated (39.6° C.), but often it is normal until just before death, when it suddenly sinks.

In the kidneys also the epithelium undergoes considerable fatty degeneration; in consequence of this the excretion of urine becomes less and less, and it soon contains blood and albumen; in consequence of the icterus the urine also contains the coloring matter and acids of bile. The other changes in the urine we shall consider under the head of transformation of materials in the body.

The symptoms due to disturbances of the nervous system are least characteristic. Consciousness is generally retained until death. Somnolence, delirium, and coma do not occur until near death, and should be considered not as primary but as secondary conditions due to the weak condition of the heart, icterus, etc. Histories of these patients also speak of pain in the head and along the vertebral column, anæsthesia of the skin, dilated pupils, disturbances of the facial and auditory nerves, etc.

Influence of Small and Large Doses of Phosphorus upon the Transformation of Materials in the Body.—Under the influence of phosphorus, the decomposition of albumen goes on with greater rapidity while the oxidation processes are diminished.

Bauer and Voit, after starving a dog for several days, and allowing the amount of nitrogen excreted to become constant, gave him small doses of phosphorus. A great increase in the amount of urea excreted (almost three times as much as normal) was the result. The investigations of Lebert and Wyss, Panum and Storch, gave similar results. There was a diminution of 47% in the amount of carbonic acid, and 45% in the amount of oxygen excreted. Bauer concludes from these observations that owing to the quantity of albumen decomposed, a large amount of fat is produced, which, from the want of oxygen, is not burnt up, and therefore gives rise to fatty degeneration of the organs. The source of the fat in the dogs, spoken of above, some of which were starved for 12 days, can be nowhere else than in the organic albumen. Even the nitrogenous products of decomposition are not entirely converted into urea, but stop at a certain stage of the process of conversion. This is shown by the fact that leucin and tyrosin are found in the organs and blood of dogs fed on phosphorus.

Schultzen and Reiss found that the appearance of general symptoms after a fatal dose of phosphorus in men, was fol-

lowed by a great diminution in the percentage of urea. In place of the urea, other abnormal nitrogenous materials appeared, which a careless observer might mistake for an increased percentage of urea.

In fatal cases, they found, as Kohts had already found, sarcolactic acid. They did not calculate the whole amount of nitrogen present in the urine, but they seemed to be of the opinion that the amount of nitrogen excreted was not changed by phosphorus, which we believe has been disproved by Bauer.

Schultzen and Riess came to the same conclusion reached by Voit, namely, that the albuminoid bodies in the organism were indeed decomposed into nitrogenous and free components, but were not oxidized into the normal final products. The diffusible products of decomposition as well as the peptonoid substances and lactic acid, are excreted, while the colloids, such as the fats, are piled up at the place of their formation.

THERAPEUTIC APPLICATION.

Phosphorus has frequently been an important drug in therapeutics, but the dangerous remedy has always again been rejected, because its manifold recommendations have never been confirmed by experience.

Thus it has been recommended as a stimulant for typhoid conditions, also lately in various diseases of the nervous systems, both in the so-called neuroses (neuralgias) as well as in gross lesions of the nervous system. It has also been recommended for leucæmia, etc.

Many experienced neuro-pathologists speak of its use in neuralgias, without expressing any personal opinion as to its value. We ourselves confess that we have never used this drug in these conditions.

The findings of Wegner have lately given a firm physiological basis for a further therapeutic utilization of this drug. That is to say, phosphorus ought to be of use in several of the pathological conditions of the osseous system, especially in rachitis, slow formation of callus, after resections, for caries and osteomalacia. Whether it will be found of any benefit in the latter condition appears somewhat doubtful. It is also a question whether the administration of this remedy to children, who are the subjects of the rachitic process, would not be somewhat dangerous. All these questions, however, can only be settled by clinical observation and experience, which is still wanting.

For external application phosphorus is entirely superfluous.

Dosage and Preparations.—1. Phosphorus—from 0.001–0.005 per dose (ad 0.015 per dose ! 0.05 per day !) dissolved in alcohol, ether, or the fixed oils, and given in mucilaginous drinks (in vitro nigro). Or, better still, it may be given in pills (with gum arabic and pulv. tragacanthæ). According to Wegner it should be given 3 times a day to the extent of 1½ mgm.

2. Oleum phosphoratum. 1 to 80 of ol. amygdal., an entirely superfluous preparation.

Treatment of Phosphorus Poisoning.—The chief object in the treatment of acute phosphorus poisoning during the first 24 hours, should be to get rid of the poison from the stomach, either by means of an emetic or stomach-pump. The bowels should be moved by means of cathartics, (but not oily ones) or clysters. Since the fats and fatty oils facilitate the solution, and therefore the absorption of phosphorus, therefore they, as well as milk and the yolk of eggs, should be avoided. Mucilaginous drinks, however, may be administered. Bamberger recommends the sulphate of copper as an excellent emetic. But here this drug not only acts as an emetic, but its administration should be continued in small doses as a direct antidote. The phosphorus, even in the form of vapor, reduces cupric sulphate, forming a more insoluble, and therefore harmless, copper phosphide. Another antidote is oxygenated (old) oil of turpentine. Concerning the utility of this H. Kohler has made a series of investigations. We refer to the chapter on oil of turpentine. 1–2 grms. of this oil should be given every ¼ or ½ hour until 5–10 grms. have been used. The other antidotes which were formerly used, such as magnesia usta, liquor chlori, etc., are no longer used, because they have shown themselves less useful than those already mentioned.

If the phosphorus has already been absorbed, we must treat the symptoms as they present themselves, such as collapse, gastritis, etc. How far transfusion may be of use, we cannot judge until we have sufficient practical experience.

ANTIMONY—ANTIMONIUM S. STIBIUM.

All of the soluble and absorbable antimony compounds have the greatest similarity in their general physiological action. This action, again, is very similar to that of arsenic and phosphorus, both as far as the symptoms and organic changes are concerned. Of the many preparations formerly recommended only three are now therapeutically used ; and even the reputation of these is constantly diminishing.

I.—TARTRATE OF ANTIMONY AND POTASH—ANTIMONIO-POTASSIUM TARTARICUM.

The tartrate of antimony and potash $2\ (C_4H_4K(SbO)\ O_6) + H_2O$ (frequently known as Tartarated Antimony and Tartar Emetic), is obtained in transparent crystals, which effloresce in dry air and lose their transparency. It is easily soluble in water—insoluble in alcohol. Watery solutions of this substance are easily decomposed by alkalies or tannic acids, which precipitates the antimonious oxide or tannate of antimony.

PHYSIOLOGICAL ACTION.

Nobiling has attempted to prove for this salt, as was proved by others for the potassium bromide and iodide, that the effect produced upon the nervous system and heart by these double compounds is due to the potash, while the gastro-intestinal action is to be ascribed to the antimony. His results from experiments made upon warm and cold-blooded animals have been disproved. According to Buchheim, Radziejewski, and others, all other soluble antimonial compounds which do not contain potassium have still a similar effect to that produced by tartar emetic upon the heart and nervous system. Such compounds are the tartrate of antimony, tartrate of antimony and soda, and various combinations of antimony and chlorine. Again, we know that quantities of potassium as small as those contained in emetic doses of tartar emetic, do not of themselves have any effect upon the heart of warm-blooded animals, while Nobiling found that even less than emetic doses of this compound (0.001—0.01 grm. in maximo) produced these effects upon himself.

ACTION OF THE DRUG UPON THE ORGANISM.

Tartar emetic is absorbed, probably unchanged, by the unbroken skin and all mucous membranes ; unchanged, for it is only with great difficulty decomposed in the gastric juice, and only after a long time in the alkaline intestinal secretion. But most of the drug is wasted, as far as any general action is concerned, since large quantities are vomited, while smaller quantities become insoluble when decomposed and are then passed off with the fæces.

After injection under the skin or directly into the blood tartar emetic may be excreted from the blood upon the mucous membrane of the stomach, or with the bile into the intestine, and can cause vomiting just as though given by the stomach. Its final excretion takes place through the kidneys, and partly with the perspiration ; but even weeks and months after the use of antimony it is said to have been found in the internal organs, as for example in the liver and the bones. (Taylor, Millon and Laveran.)

GENERAL SYMPTOMS RESULTING FROM THE USE OF TARTAR EMETIC.

When tartar emetic is given to a healthy person once a day

for some time, in very small doses of 0.001 grm., and gradually increased to 0.01 grm. (that is to say in doses that do not cause vomiting), the following symptoms will present themselves, as observed by Meierhofer and Nobiling upon themselves: Depression of spirits, heaviness and fullness of the head, weariness of the limbs, tearing and dragging in the joints, febrile chilliness, accumulation of the saliva in the mouth, thickly coated tongue, thirst with an internal feeling of heat, rush of blood to the head, sleepiness, sleep disturbed by dreams, increased frequency and irregularity of the pulse, dizziness, flickering before the eyes, pale, depressed countenance, blue rings around the eyes, increased collection of mucus in the throat, and difficulty in swallowing.

When taken for a still longer time the drug produces diminution of the appetite, pressure in the stomach, sharp and frequent pains in the intestine, nausea, anxiousness, frequent yawning, difficult respiration, and an exceedingly anxious feeling over the heart and chest. The abdomen is tense and painful to touch. There is a sensation of chilliness all over the skin. Sometimes there is diarrhœa, and at other times constipation. The excretion of the urine is increased, not in consequence of the drug but on account of the increased amount of water which has been taken. The pulsation of the heart becomes weaker and slower. The apex beat is perceived over a greater area, but less intense than normal. The face has a sickly color. The whole body appears thinner than normal.

If the 0.01 grm. doses do not now cease to be given, but are continued, the above symptoms grow worse and worse. The nausea leads to regurgitation and severe vomiting. The stools become more frequent, thin, slimy, and are tinged with bile. The area of dullness over the liver is increased, while there are pains always present in the liver. There are constant rumbling and pains in the abdomen. Itching of the skin is noticed. There is a constant increase in the excretion of mucus. The stasis in the pulmonary circulation begins to be felt in the chest.

The appearance of albumen in the urine prevented Nobiling from continuing the experiments upon himself; this had already been observed by Meierhofer. The bodily weight had diminished by 3½ kilos. during the fourteen days of the experiment. Not until three days after discontinuing the remedy did the appetite return, and it was two months before all of the after effects disappeared.

In large dose (above 0.1 grm.) the drug produces symptoms

of gastro-enteritis very similar to those following arsenical poisoning. There are severe pains along the œsophagus and in the abdomen, accompanied by vomiting and later on severe purging. The vomiting is accompanied by a great loss of strength, which may result in syncope or even death. The pulse is thread-like, rapid, almost imperceptible, and irregular; there is sighing respiration and difficulty in maintaining the erect posture; the skin is cold, and covered with a clammy sweat; there is considerable cyanosis.

Cases have been observed in which only collapse, without gastro-enteritic symptoms, have occurred.

The smallest fatal dose for adults is on an average 0.5 grm., but even smaller doses give rise, as we have shown above, to very serious symptoms, or if the heart be already affected, even death. It was the ancient practice to give very large doses (15 grms. and over); it was asserted that in inflammation the patients bore these enormous doses well. Although this assertion is not well founded, yet we will not deny its possibility. Febrile affections, for example, may so diminish the absorbtive power of the intestine that little antimony gets into the blood; or the nervous system may react differently under the influence of high temperatures than it does under the normal temperature. In some cases a large part of the drug is immediately expelled by vomiting. But it is also possible that larger doses, by paralyzing reflex action, may have a directly opposite effect from that of emesis. All of these, however, are only unproved possibilities. Under any circumstances, we should condemn the use of such large doses of antimony, since we know that when the drug is absorbed into the blood it produces severe organic changes.

INFLUENCE OF ANTIMONY UPON THE TISSUE ELEMENTS AND THE INDIVIDUAL ORGANS.

As was the case with phosphorus and arsenic, so with tartar emetic; we find that it has no especial chemical influence upon albumen. It has not been shown to precipitate dissolved albuminates (except upon the addition of free oxide to the albuminous solutions), nor does it withdraw water from the tissues.

The inflammatory symptoms are too slow in their production to be considered the result of any escharotic action. *Hermann* calls attention to the fact that the drug produces inflammatory symptoms not only locally, but even at a distance. Thus ulcers of the stomach follow the application of the drug

to the skin; while ulcers of the skin result from the internal administration of the drug, under which circumstances the drug would certainly have had an opportunity to satisfy its affinities in passing through the blood before it reached the skin.

Skin.—The direct application of this drug to the skin produces a pustular eruption resembling that of small-pox. Sometimes this eruption becomes confluent, the pustules penetrate deeply into the skin, and in healing leave distinct scars.

According to Falck this eruption does not occur at all, or occurs much later, when the nerves of the skin are paralyzed. It seems to originate in the glands of the skin, by causing the production of an acid substance in their secretion; for when introduced into deep wounds of the skin or when mixed with alkalies, tartar emetic is said not to produce any pustules, while the addition of acids to the drug causes the eruption to be more severe. We have already mentioned that this eruption may follow the internal administration of the drug.

Mucous Membranes.—Here also we may have the appearance of a pustular eruption resulting from the swallowing of solutions of tartar emetic. This eruption may extend from the mouth to the stomach and is generally preceded by a catarrhal inflammation of these mucous membranes. Nobiling asserts that these ulcers frequently occur, after the long-continued administration of small doses. The Munich anatomical collection possesses a large number of such specimens. The administration of a single emetic dose of the remedy does not produce in animals inflammation of the gastro-intestinal mucous membrane, but only loosening and separation of the epithelium (Handfield-Jones.)

Explanation of the Emetic Action of this Drug.—Hermann and Grimm observed that in dogs larger doses of tartar emetic were needed to produce vomiting when the drug was injected into the blood or under the skin, than when the remedy was introduced into the stomach. It would be unexampled that substance acting directly upon the brain should have less influence after direct injection into the blood than when given by the stomach. It was therefore supposed that the action of the drug was either directly or in part a peripheral one, and that it exerts an irritation upon the walls of the stomach and the nerves terminating there which causes vomiting by a reflex act. Indeed it was necessary to suppose that even when injected into the blood only those portions which reached the walls of the stomach or were excreted by its glands

were active in producing vomiting. Radziejewski and the above-named authors showed that after injection into the blood the largest part of the salt was found in the vomited matter. Magendie's experiments upon animals, in which he extirpated the stomach and yet caused the movements of vomiting by the administration of tartar emetic, are not contradictory to the above mentioned facts; they only show that there may be other peripheral nerve terminations in the pharynx or œsophagus perhaps, the irritation of which gives rise to vomiting. Gianucci's discovery that when the upper part of the spinal cord is cut, tartar emetic does not produce vomiting, cannot be taken to prove that the cause of the vomiting is central, if only for the reason that no drug can produce vomiting in animals that are gagged, bound down on the back and kept alive by artificial respiration, although if loosened and allowed to stand upon their feet in the normal manner they might vomit.

Fatty degeneration of various organs, such as the liver and muscular tissue of the heart, occurs after antimony as well as after phosphorus and arsenic (Saikowski). Even after smaller doses which were continued for a long time Nobiling observed enlargement and tenderness of the liver. The occurrence of the venous hyperæmia of the liver, spleen and kidneys, etc., Ackermann accounts for by the weakness of the heart's action and the stasis of the blood in the venous system which results therefrom. The stasis in the kidneys may be the cause of the albuminuria.

Circulation and Temperature.—The influence of this drug upon the heart's action can only partly be the reflex result of the irritation of the nerves of the stomach (the branches of the vagus). Its chief cause must be the direct action of the salt.

In cold-blooded animals 0.05 grms. produces a temporary (15 minutes) increase, followed by a diminution, in the number and force of the pulsations of the heart.

In warm-blooded animals (dogs) the force of the heart and the blood pressure are diminished from the beginning, the number of pulsations on the whole is diminished, although sometimes there is a temporary increase. Finally the heart's action becomes irregular, and the heart stops (after fatal doses) in diastole.

In man during the period of nausea the pulse increases in frequency by about 40 beats; later on, however, the frequency *diminishes*. During the stage of reaction, when the vomiting is over, the force and number of the pulsations is soon increased.

This is a proof that a portion of the cardiac symptoms is dependent upon a reflex action.

That a large amount of venous hyperæmia occurs in all the organs, simultaneously with the diminution in the force of the heart, we have already stated.

The temperature falls in direct proportion to the diminution in the force of the heart's action 6.6°C. (Ackermann and Radziejewski).

Nervous System and Voluntary Muscles.—In warm-blooded animals it is difficult to decide how much of the effect upon the nervous centers is due to the changes in the circulation, and how much to the direct action of the poison. Under any circumstance we must consider that the chief part of the effect is due to the former cause. But since in cold-blooded animals, in whom the nervous system is much less dependent upon the circulation, tartar emetic causes paralysis of the cerebro-spinal centers and complete loss of reflex irritability, and since in rabbits (who cannot vomit) the same effect was observed (Radziejewski), we must consider that in warm-blooded animals also the drug has a direct influence upon the brain and spinal cord. It is possible that the final paralysis of the spinal cord explains why the continued administration of large doses is not followed by vomiting.

A diminution of muscular power has been observed as a rapid effect of tartar emetic in men and animals. Even very strong and wild animals fall down weak and exhausted after the administration of this drug; at most they can make a few steps only again to fall down. Sometimes muscular tremor sets in. Immediately after the vomiting this condition improves somewhat only to return again in an aggravated form. There can be no doubt that this condition is in a great measure due to a direct alteration in the function of the muscular and nerve tissue. Experiments upon the muscles of frogs show no change in the form of the muscular contraction curve, but an extraordinary depression of the same (Buchheim).

The respiration in warm-blooded animals and men is at first hastened, superficial and irregular, later on stertorous with a quick, snapping and very difficult inspiration, and a long, resounding expiration.

These symptoms are to be looked upon as the reflex result of the disturbance of the stomach, as they always set in after vomiting from whatever cause. Indeed the movements of vomiting are nothing more than abnormal respiratory movements.

The assertion of the older authors of great changes in the lungs and hepatization of the same after the use of tartar emetic is contradicted by Ackermann, who bases the contradiction upon twenty post mortem examinations of dogs killed by this salt. Whether the increase of mucus in the bronchi is the direct result of the action of the poison or a consequence of the venous stasis in the pulmonary circulation has not been determined.

The collapse which is a prominent and constant element in the effect of tartar emetic, is probably due, to a great extent, to the enormous diminution in the blood pressure and weakness of the heart produced by this drug. This is the cause of the pale, livid appearance of these patients, of the cold surface, and partly, perhaps, of the affection of the muscles. Ackermann calls attention to the fact that a similar condition always accompanies nausea, even when poison is not the cause of it; as for instance in sea sickness.

We have no positive observations as to the effect of this drug upon the various secretions.

Tartar emetic exerts an influence similar to that of phosphorus and arsenic upon the interchange of materials going on in the body. When the amount of nitrogen excreted by starving animals has become constant, the administration of this poison causes an increased excretion of nitrogen.

Paralysis of the heart is the cause of death in all or most of the cases.

THERAPEUTIC APPLICATION.

The large number of diseases in which tartar emetic was formerly used, has gradually become diminished until personally we have no hesitation in declaring that the only internal application of tartar emetic which we consider firmly established is its use as an emetic.

Tartar emetic is used as an emetic principally in combination with ipecacuanha. The indications for this application of the drug are the ordinary ones. Its effect is pretty certain. The action which it exerts at the same time upon the intestine and heart, however, is very disagreeable. Collapse following the use of tartar emetic is often very considerable and therefore the remedy should be used with great care in children, debilitated individuals and old people.

Of the many acute inflammatory and febrile affections in which it was formerly given, tartar emetic is still used in acute

bronchitis. It should be given whether the affection be recent, or whether it be an acute exacerbation of an already existing catarrh, when cyanosis and fever are present and when the physical examination reveals coarse rhonchi and whistling râles and but few sibilant râles. In such cases it should be given at first in emetic doses and later on in small doses. Necessary conditions for its use are that the patient be strong and that no complication on the part of the digestive canal should be present; if these conditions are not fulfilled tartar emetic is injurious. We would call attention to the fact that this drug should not be used in secondary catarrhs, even if its use be otherwise indicated. Such secondary catarrhs are those which accompany typhus. The reasons for abstaining from its use in this disease will be evident from what has been said. We have attempted to formulate these conditions more accurately in order to warn against the misuse of the remedy in other forms of catarrh. We must confess, however, that even in cases in which the above indications are present, we have less and less confidence in the utility of this drug. People who suffer from acute febrile bronchitis generally take to their beds, are kept in an equable temperature, and have blisters, cataplasms, etc., applied. Under these circumstances we could only consider that tartar emetic had been useful when the various symptoms of catarrh had rapidly and immediately disappeared under its use; if this is not the case we would ascribe the improvement to the action of the other agents. Nor have we seen any very rapid improvement follow the use of this drug.

This closes the series of the therapeutic indications for the use of tartar emetic, for in croupous pneumonia, in which it was formerly given very frequently, it is to-day scarcely used by any physician, so that we shall not enter upon any discussion of this use of the drug. In the large number of other inflammations in which tarter emetic was recommended, as, for instance, in inflammations of serous membranes (pleuritis, pericarditis, etc.,) as well as in articular rheumatism, it has not shown itself of any utility. In other conditions, also, in which it was formerly lauded, that is to say in gastric, rheumatic and simple catarrhal fever, it is no longer given in small doses, and is only used when an emetic is indicated and tartar emetic is selected as a proper one. Its administration in mental diseases in nauseous doses (nausea cure) is only interesting from a historical point of view.

Externally tartar emetic is used with questionable benefit as a severe cutaneous counter-irritant in inflammations of internal

organs, especially in meningitis (upon the shaved scalp), laryngitis, tracheitis, and less frequently in other conditions. Formerly it was generally recommended (Jacobi and others) to apply the tartar emetic ointment to the shaved scalp of patients suffering from psychical diseases. This application of tartar emetic was, until very recently, entirely abandoned. But L. Meyer again recommends it and pretends to have cured even patients affected with dementia paralytica.

Dosage and Preparations.—1. Antimonio-potassium-tartaricum internally, in divided doses, from 0.005–0.03 every two hours in solution (0.05–0.3 to 150–200), mixture or powder (ad 0.2 pro dosi! ad 1.0 pro die). On account of its readiness to decompose, all chemically incompatible substances should be avoided in these mixtures. As an emetic it should be given in from 0.03 to 0.1 doses at intervals of ten or fifteen minutes. Tartar emetic is rarely given alone for this purpose, but generally in combination with ipecacuanha (see this drug) either in mixture or powder. As an emetic for children we may give from 0.005 to 0.02.

Externally it is rarely used as a wash (0.25–1.0 to 30.0) but generally in the form of an ointment (for mild irritation 1 to 3 parts to 30 parts; for the production of pustules 1 part to 4 to 8 parts) or in the form of a plaster, 1 part to 5 parts of the plaster mass. For clysters which are to have an emetic effect the proportion is 0.3–1.0 to 150–200. For injecting into the veins (for an emetic effect) 0.05–0.25 to 30.0–120.0. Other methods of application are no longer followed.

2. Vinum antimoniatum, s. emeticum, s. antimonio-potassii tartarici, wine of antimony, 1 part of tartar emetic to 250 parts of vin. xericum; a clear, dark-yellow solution. Rarely used as an emetic for adults, but mostly only for children; as an emetic a teaspoonful every quarter of an hour (often given in combination with oxymel scilliticum).

3. Unguentum tartari antimoniati, s. antimoniatum, s. antimonio-potassio tartarici. Pustule ointment; 1 part of tartar emetic to 4 of adeps. Very white. A piece the size of a pea to be rubbed in twice daily.

Treatment of Antimonial Poisoning.—No emetics are here indicated, since the poison itself acts as an emetic and cathartic. Until antidotes can be obtained, we should give simple mucilaginous drinks (and perhaps tea or coffee). The best antidotes are materials containing tannic acid, which forms quite an insoluble compound with antimonious oxide. Such are tannin, a strong infusion of nut galls, or quinine. If the emesis continue, effervescing drinks and opium may be given. The gastro-enteritis and collapse should be treated in the usual manner.

2. THE PENTA-SULPHIDE OF ANTIMONY—ANTIMONIUM SULPHURATUM AURANTIACUM.

The penta-sulphide of antimony, Sb_2S_5 (known under the old names of golden sulphur and auratum antimonii), is best obtained by decomposing, by the aid of sulphuric acid, the sodium sulphantimoniate (Schlippe's salt). It is a fine orange-yellow odorless powder, soluble in water and alcohol, and decomposable by heat into the tersulphide of antimony and sulphur.

Physiological Action.—This compound, like all other antimonial compounds which are insoluble in water, can only exert a physiological action

when it is decomposed in the body and changed into soluble salts. It passes through the mouth entirely unchanged, and is therefore without taste unless it is contaminated by sulphuretted hydrogen (which is frequently the case). The changes which it undergoes in the stomach are not well understood, but it must be supposed that soluble combinations are formed, for it produces effects very similar to those of tartar emetic only less certain and less intense. It would therefore be useless to repeat what has already been said when considering tartar emetic, and in practice it will be found better to make use of the small and certain doses of the latter drug than to depend upon this uncertain preparation.

Therapeutic Application.—The antimonic sulphide is an entirely superfluous preparation. It is true that it is still used as an expectorant, but its utility is held in very low estimation, if not entirely doubted. A necessary condition for its use is a good appetite. If this be present it may be given in the same conditions in which we would use sal ammoniac.*

In all other conditions, however numerous they may be, in which this drug has been recommended since the time of Glauber and Fr. Hoffmann (who were the first to warmly recommend its use), it is just as superfluous and ineffective. Thus it was formerly much prescribed in scrofula (especially for the accompanying exanthemata and swelling of the lymphatics).

Dosage and Preparation.—Antimonium sulphuratum aurantiacum (from 0.02 to 0.1, pro dosi every two to four hours), in powder, pill, troches or mixture. Inasmuch as this compound is readily decomposed it should be given only in as simple a form as possible ; we should especially avoid combining with it acids, alkalies, haloids and metallic salts.

Note.—Equally superfluous is the antimonium oxidatum (antimonous acid anhydride Sb_2O_3) and also the so-called antimonium sulphuratum rubrum (Kermes mineral) which is an uncertain mixture of the tersulphide of antimony with antimonium oxide. Finally also the antimonium sulphuratum crudum and laevigatum (Sb_2S_3).

3.—ANTIMONIUM CHLORATUM SOLUTUM.

The liquor antimonii chlorati (sometimes called butter of antimony, although not very aptly, since it is of an oily appearance), is formed by the solution of antimonium oxide or the tersulphide of antimony in concentrated hydrochloric acid ; thus is formed the $SbCl_3$. It is a yellowish oleaginous fluid, whose irritant effect is mostly dependent upon the hydrochloric acid which it contains. It is but little used, and best replaced by the caustic alkalies. The indications for its use are the same as those for the latter.

BISMUTH—BISMUTHUM.

The soluble bismuth compounds (as for example the acetate, the citrate and ammonia-bismuth) have, according to Lebedeff, Stefanowitsch and Feder-Meyer, an intensely poisonous action which resembles that of arsenic and antimony, in that it causes fatty degeneration of internal organs and disappearance of glycogen from the liver. These compounds, however, are not officinal in the German Pharmacopœia, and have never been used therapeutically.

* See page 112.

It requires considerable self-control for us to introduce in a scientific work the basic bismuth nitrate, or bismuthum subnitricum, magisterium bismuthi $No_3(BiO)+Bio—OH$ as well as the bismuth valerianate—bismuthum valerianicum.

Physiological Action.—Both preparations are entirely insoluble in water. Concerning the valerianate we have no knowledge, while the basic nitrate leaves the body with the fæces, without loss, because it is entirely unabsorbable. The only positively determined effects are the black color which it imparts to the fæces by the formation of bismuth sulphide, and perhaps slight constipation in consequence of the dryness of the fæces (Monneret-Trousseau). The contradictory opinions as to its action which were held in former times, and according to which it was said to be a violent poison, were probably due to the impurities of arsenic and lead which contaminated the preparations of this drug.

Therapeutic Application.—We are decidedly of the opinion that the basic bismuth nitrate (as well as the valerianate) should be stricken from the number of therapeutic agents.

In the conditions in which the utility of this preparation was dependent upon its supposed absorption, it has for a long time past not been prescribed, because it is understood that it is not absorbed—such conditions are epilepsy, chorea and whooping-cough. On the other hand, it has for the last hundred years maintained a reputation for being exceedingly useful in diseases of the digestive canal. We ourselves have not administered the remedy for many years, either in cardialgia, whatever might be its ætiology, or in ulcus ventriculi, or in gastric catarrh, without having had any worse therapeutic results than others who have used it. Other observers maintain the same view (Leube, etc.)

The mere fact that we could not explain its utility in cardialgia would be of little importance, for this objection would hold good for many drugs which experience has shown to be valuable. But why should we conceive that the effect is due to this drug, when the preparation is almost never given alone, but in combination with other active substances, such as morphine, belladonna, etc., and when the diet is strictly regulated, and finally, when the same effects are sure to follow, without the giving of any bismuth. On the other hand, the fact that the drug has been used for years, is of no moment, for the history of the science of materia medica shows what little weight should be attached to this fact.

Since then the physiological effect of the drug is almost nil (that is when the preparation is uncontaminated by arsenic) and since in our opinion there is no evidence of its therapeutic utility, and experience has shown that it can easily be spared without any disadvantage, it appears entirely useless to prescribe this drug any further.

But in order to comply with the requirements of present practice, we would add that bismuth is said to be most successful in the gastric pain of hysterical subjects; also in the gastric pains of overworked, ill-nourished and deteriorated individuals, when these are accompanied by a certain irritability of the stomach, so that eating is followed by pain and vomiting, without other symptoms of gastric catarrh being present. So also it is said to have a favorable effect upon the cardialgia which accompanies disease of other organs, and also that of pregnancy. Finally, it is used in the cardialgia of ulcus ventriculi and carcinoma of the stomach.

In addition, bismuth in recent times has been recommended in diarrhœa, especially the form depending upon an ulcerative process in the intestine.

According to Traube, its action is to be explained on the supposition that it forms a protective layer over the surface of the ulcer, diminishing the irritability of the exposed sensitive nerve ends and thus decreasing the number of the reflex peristaltic movements. That it is to be preferred in these cases to other remedies has not been proved.

Dosage.—Bismuth. subnit. and valerianat., 0.3–0.5 in powder. French physicians give up to 15.0 per day.

NITROGEN—NITROGENIUM.

Nitrogen, together with oxygen and a little carbonic acid, are the principal ingredients of the atmospheric air. (79% by vol. of N. to 20% by vol. of O., and 0.04% by vol. of CO_2).

It is an odorless, colorless and tasteless gas, non-condensible, and non-inflammable and does not support combustion.

Physiological Importance and action.—Free nitrogen enters the body with the air that is inspired and absorbed, and is but little absorbed by the blood (about 2% by volume).

When this gas is inspired together with the oxygen, it has almost no physiological effect, and at most acts as a diluent of the oxygen.

When the pure gas is inspired no disturbances result from it, but only from the want of the oxygen, which it replaces; and the rapid loss of consciousness which results in warm-blooded animals is due to this; if this lack of oxygen be continued, we have a stoppage of all of the functions and death as a result. Since during the inspiration of nitrogen, the expiration of the carbonic acid that is formed in the body continues, we have an entire absence of the symptoms of carbonic acid poisoning which are apt, under other circumstances, to obscure those due simply to the want of oxygen. Cold-blooded animals live in a pure nitrogen atmosphere for a long time, since they can bear the loss of oxygen for some time, and the nitrogen has no deleterious effect.

Treutler, who makes use of the inhalation of nitrogen gas in diseases of the lungs, especially in phthisis, manufactures the N. gas in the following manner. The atmospheric air is allowed to pass over iron turnings which have been moistened by ferrous sulphate; this salt is oxidized by absorbing the oxygen of the air; the oxygen so absorbed is again entirely passed over to the metallic iron while the salt remains at its lower grade of oxidation as long as any metallic iron exists. In this manner the nitrogen is obtained from the air. Treutler allows the gas to pass into a pneumatic apparatus, which permits of various admixtures of the nitrogen with atmospheric air, whence the mixture is inhaled by the patient. Generally the quantity of oxygen supplied to the patient is diminished by from 5–10%. Theoretically this method of treating phthisis seems to promise little. There is as yet no extended practical experience of its use.

NITRIC OXIDE—NITROGENIUM OXIDATUM.

Nitric oxide gas, NO, immediately combines in the air with oxygen, and forms nitrous acid anhydride, N_2O_3, and hyponitrous acid, $NONO_2$. The addition to and abstraction of the atoms of oxygen fromsnitrogen, if in the presence of animal tissues, produces in them severe disturbances. The severe effects of the inhalation of these compounds are seen immediately at the point of entrance, where they produce a reflex convulsive closure of *the glottis,* and as a result, suffocation. Nitric oxide cannot therefore be in-

haled, and for this reason can produce no further general effects. The internal effects of the nitric oxide upon the tissues, however, can be studied by the administration of the sodium nitrite, which exerts an action similar to that of arsenicupon the body. Paralysis of the nervous system, congestion of the intestinal canal, etc. (Binz).

If nitric oxide be allowed to pass through blood, oxy- or carbonic oxide hæmoglobin solutions, the oxygen and carbonic oxide are replaced by the nitric oxide, and we have a nitric oxide-hæmoglobin combination formed; this again can be replaced by hydrogen gas. Nitric oxide is not used therapeutically.

NITROUS OXIDE—NITROGENIUM OXIDULATUM.

Nitrous oxide N_2O (nitrogen monoxide—laughing gas—is a coloress gas, having a slight odor and sweet taste; it supports combustion almost as well as oxygen does, and is condensible and slightly soluble in water.

PHYSIOLOGICAL ACTION.

If a mixture of nitrous oxide and oxygen be inhaled for several minutes (80 vol. of N_2O+20 vol. O) there is produced, according to Humphrey Davy and Hermann, a condition resembling that of intoxication, with the following symptoms: roaring and ringing in the ears, indistinct vision, an increased subjective sensation of warmth and a feeling of extraordinary lightness in all the limbs. All intended movements are exaggerated in extent. There is considerable swaying of the body when sitting, and in walking there is stamping of the feet, touch is unaffected, but sensation of pain is undiminished. Cerebral activity is increased; the patient is livelier, he laughs and rejoices. Consciousness is never entirely lost. During the whole of the experiment there is reddening of the face and conjunctiva, while there is a moderate increase in the pulsation of the heart. In the mammalia this narcotic effect is shown by a lowering of the tonic irritability of the vagus (diminution in the frequency of the respiration, and increased frequency of the pulse—Zuntz–Goltstein).

According to Bert, the inhalation of a mixture of nitrous oxide and oxygen, under pressure, results in a very short time not only in intoxication but in anæsthesia.

When the inhalation is interrupted, complete restoration sets in in a very short time.

Pure nitrous oxide, which is free from oxygen, produces, according to Hermann, the above symptoms of intoxication very rapidly in man. At the same time, however, dyspnœa sets in, consciousness is almost entirely lost, and after asphyxia has set in the heart ceases to beat. The face becomes pale as a corpse, and the mucous membrane cyanotic. The suspension

of the sensation of pain and the commencement of cyanosis generally go together, so that when the latter is present the first may be suspected. If the narcotism is not carried beyond this stage, consciousness and a return to the normal state occur in about a minute. On the other hand, if the respiration has been stopped and the heart has ceased to beat, life can only be restored by artificial respiration. Warm-blooded animals, to whom the gas has been administered for a certain length of time, die after severe dyspnœa and convulsions due to paralysis of respiration. In these cases the blood is of a dark, venous color. Cold-blooded animals live in this gas, as they do in other indifferent gases*, for a great length of time.

To the conclusions of Hermann, we (Rossbach) have to add the following, as far as rabbits are concerned : During the dyspnœa the blood pressure in these animals is very much increased, and the heart's beat is slower but stronger.

Three minutes after the inhalation of the gas the movements of respiration cease (asphyxia). The pulse becomes slower, arhythmical, and always weaker until it finally ceases two minutes after complete asphyxia. In order to see after how long a time life can again be restored, we did not attempt artificial respiration until the animal had lain dead two to five minutes. Even after five minutes life was restored, and a return of all the functions to the innormal took place in a very short time. This is a further proof of Hermann's view that nitrous oxide acts as an entirely indifferent gas upon most of the functions of the body, especially upon the respiration and circulation.

On the other hand, the intoxicating effect of nitrous oxide, mixed with nitrogen, shows that the ganglia of the gray substance of the cerebrum are directly affected by the gas, and that it has not merely an indifferent action upon this organ. Nitrogen and hydrogen do not produce such cerebral symptoms. The manner and method of this influence of nitrous oxide upon the cerebral ganglia is as little known as are the methods of action of all other narcotics. Complete anæsthesia, which is produced by the inhalation of nitrous oxide gas, is therefore the result of a combination of its narcotic and suffocating action. That suffocation is not the only method of its action is shown, according to Zuntz–Goltstein, by the fact that frogs lose their reflex irritability in nitrous oxide in a few minutes, while in hydrogen it is only lost after a few hours.

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* See page 261.

The dyspnœa which occurs while suffocating one of the mammalia with nitrous oxide gas is much less in degree than that which follows suffocation by an indifferent gas. In the former case convulsions are either entirely absent or are only very slight. At the occurrence of anæsthesia suffocation has not advanced as far in man as in dogs or rabbits (Goltstein).

As in ordinary suffocation so in the inhalation of nitrous oxide, we can recognize three stages of dyspnœa. 1st, a stage in which inspiratory efforts predominate. 2nd, a stage, characterized by labored and active expiration; and 3d, a stage, in which the inspirations become fewer and shallower, until paralysis of the respiratory center sets in. Since loss of sensibility during inhalation of nitrous oxide sets in toward the end of the second stage, and lasts from one to two minutes, even if the patient be allowed to breathe air immediately, there can be no danger from the respiratory center by the use of this agent for the production of anæsthesia (Zuntz).

The increase in blood pressure which always accompanies suffocation also occurs during the inhalation of nitrous oxide, but never attains any considerable height. When the narcotism is repeated, however, a second increase in blood pressure occurs which frequently attains a higher degree. In cases, therefore, in which there is danger of an easy rupture of the vessels, the narcosis produced by nitrous oxide might easily become dangerous. A similar result, however, might be produced, apart from the narcosis, by the increase in blood pressure which results from the pain of the operation (Zuntz).

Nitrous oxide does not undergo any chemical combinations in the blood, but is simply absorbed. The serum of the blood has, however, no greater absorptive power for the gas than pure water. When blood is shaken up with nitrous oxide it very rapidly turns of a venous color (Hermann).

THERAPEUTIC APPLICATION.

Nitrous oxide has been very widely used for several years, but almost exclusively as an anæsthetic in dentistry, especially for the extraction of teeth. Since, as we have already stated, the anæsthesia only lasts from one to two minutes, it can only be used in such operations which can be finished in a similarly short period. Even then it requires a practiced surgeon to perform a difficult extraction of a tooth in this space of time.

The gas should be given pure, without admixture with at-*mospheric air.* We cannot take the time to test the loss of re-

flex irritability in order to determine the proper moment for beginning the operation, for meanwhile the anæsthesia might be over; but the tooth is extracted as soon as the respiration begins to be labored, and the face and nails become cyanotic.

The commencing cyanosis certainly has a serious appearance to those looking on, but experience has shown that the production of anæsthesia by nitrous oxide is without danger. Whether a few individual accidents should be taken as a contra-indication against the use of the gas, depends upon the importance which is attached to anæsthesia in extracting a tooth. An important reason against the general introduction of the gas into practice is the inconvenience attending its preparation, in case it is not used daily as in the practice of specialists in dentistry.

Paul Bert has recently asserted that a mixture of nitrous oxide and atmospheric air, administered under an increased pressure (by $\frac{1}{5}$), can produce an anæsthesia which lasts for a longer time—up to 30 minutes, and which is free from symptoms of excitation and asphyxia, and therefore without danger. Whether this will be confirmed, and thus prove the gas valuable for surgical practice, is a question.

Should severe poisoning, with stoppage of respiration and pulsation of the heart occur, we should not only apply artificial respiration but should immediately begin regular and forcible compression of the chest and abdomen, and thus attempt to put in motion the circulation and the respiration. The patient should lie in a horizontal position.

BROMINE, IODINE AND CHLORINE, AND THEIR COMBINATIONS WITH THE ALKALIES.

The four elements, fluorine, chlorine, iodine and bromine, are similar in their chemical properties and form a natural family of elements. Being powerfully electro-negative bodies, they have a great affinity for union with the electro-positive eleements which act as bases, such as the metals with which they form salt-like combinations, whence the name halogens. This affinity is even greater than that of oxygen. Their compounds with hydrogen have, therefore, the characteristics of strong acids.

Fluorine is, chemically, the strongest element of this group; then follow, in diminishing series, chlorine, bromine and finally iodine. The latter can, therefore, always be replaced in their metallic combinations by the former.

The physiological action of the three weaker members of this group is very similar, so that even from a physiological stand-

point we are warranted in treating of these three elements together.

Fluorine is neither of physiological nor of therapeutic importance.

The local effects of these three elements, in a free condition, upon the tissues, are entirely similar, varying only quantitatively —the chlorine, in accordance with its stronger chemical action, being here also the strongest, while the iodine is the weakest.

The combinations of these elements with the alkalies, which even in concentrated condition have only a very weak local effect, behave in a manner directly the reverse of that of the free elements, the chlorides of the alkalies having the weakest effect upon the organism, while the iodides exert the strongest action. The probable cause of this reversal of the former relation is that the chlorine is so firmly bound to its metal that it does not become free in the blood, and therefore a general chlorine action does not occur; while the bromine, and especially the iodine, become separated and free from their metals, and thus act upon the albuminoid bodies, not as indifferent salts, but as free bodies with strong affinities. Since, therefore, the iodides and bromides impart to their salts their own peculiar physiological action, we have preferred to consider these in connection with iodine and bromine, while the alkaline chlorides seemed more properly to belong to the alkalies. (See page 58.)

The diffusion power of the alkaline chlorides, bromides and iodides is a mean between that of the alkaline nitrates, as the most diffusible on the one hand, and the alkaline carbonates, sulphates and phosphates on the other. The alkaline chlorides have a greater diffusion power than the similar combinations of bromine and iodine. Taking in consideration, therefore, the greater diffusion power of potassium, we would have the following diminishing series: Potassium chloride, bromide, and iodide, and sodium chloride, bromide and iodide, of which the latter diffuse more slowly through the animal tissues (Graham, Buchheim). All of them, however, appear quite rapidly in the excretions.

THE BROMIDE COMBINATIONS.

I.—BROMINE—BROMUM.

Bromine (Br.) is only found in combination with metals, especially sodium, in sea water, salt springs, and salt deposits.

It is a dark,* blackish-red fluid, which evaporates at ordinary tempera*tures, and boils* at 50°. It is soluble in 30 parts of water, and more readily *in ether.

Chemically it is entirely analogous to chlorine, which can decompose its combination with the metals and set the bromine free.

Physiological Action.—We shall here consider the physiological action of the element bromine (which at most could only be used therapeutically as an external agent), for didactic purposes only, so that when we come to consider the potassium and sodium bromides, we shall be enabled to point out what portion of the effect is due to the bromine, and what to the potassium component of the salt.

The effect of the disagreeably smelling bromine (like that of the chlorine) upon the animal tissues can be accurately accounted for by its strong affinity for hydrogen, which it tears from the organic molecules and combines with itself to form hydro-bromic acid, thus destroying the function and structure of the original molecule. The observations of Glover seem to favor the view that bromine can also enter into a chemical combination with the albuminates.

Upon this depends the inflammatory and caustic effect of the bromine (in a fluid or vaporized condition) upon the skin and mucous membranes, together with all the symptoms of gastro-intestinal inflammation, spasm of the glottis, and the bronchitis which it produces, and of which we shall speak more under the head of chlorine.

If the bromine be administered in such large doses that its local effects upon the respiratory and digestive organs do not occur, and the picture of its general effect upon the nerve center and internal organs is not clouded, it appears, as far as can be ascertained with certainty from many contradictory observations, that bromine circulating in the blood of men and animals, even in non-dangerous and medicinal doses, has a specific action upon the cerebrum and spinal cord. This effect is seen in a diminution of the cerebral activity, reflex irritability and sensibility, and a tendency to sleep. Respiration and circulation are not sensibly interfered with.

Small and greatly diluted doses, when injected directly into the blood of animals, produces a severe irritation of the mucous membranes, more especially of the nose—at first an acceleration and finally a slowing of the respiration and heart's action ; also vomitting and diarrhœa.

Medium and large doses produce severe convulsions, which often rapidly lead to death.

Therapeutic Application.—The drug is entirely superfluous, even for external use, for which it has been recommended (as a disinfectant—locally in diphtheria, etc.), it can be replaced by other drugs.

Landolfi's caustic paste, which among other constituents, contains chlorobromine, we have already spoken of on page 160.

POTASSIUM BROMIDE—POTASSIUM BROMATUM.

Potassium bromide (KBr.) is found in sea water and in small quantities in the Kreuznacher Springs. It forms shining, colorless and odorless cubes, having a salty taste, and easy soluble in water and alcohol. To 33 per cent. of potassium we find 67 per cent. of bromine in potassium bromide.

PHYSIOLOGICAL ACTION.

The effect of potassium bromide upon the healthy and diseased organism of men and animals has been recently the sub-

ject of a large number of investigations. We shall attempt to give, as far as possible, the real results of these experiments, without entering upon the various differences of opinion. A large part of these contradictions is due to the fact that the observations upon men in health and disease, and the experiments upon animals, have not been properly differentiated.

One set of observers believe that all of the effects of potassium bromide are the result of the potassium action. This explanation, however, is no longer tenable. The specific action upon the brain and spinal cord, and upon the reflex irritability of the nerves of the gums and palate, as well as the eruption upon the skin, can now positively be explained as depending upon the bromine component of this salt. On the other hand, the effect upon the circulation, respiration and temperature is almost entirely due to the potassium action. Since these latter effects occur in animals generally after experiments with large doses of the drug, lasting at most only a few hours, and since the cerebral effects of the drug upon animals can not be a subject for investigation, it is easily seen why the experimenters upon animals believe all the effects due to the potassium, while the clinicians, who judge from the effects produced by the continued use of the drug, properly believe that the bromine plays the principal part in its action.

All doubts concerning this point are set at rest by the recent experiments of Krosz on men; these are decidedly adverse to the view that the large quantity of bromine contained in the potassium bromide (about 67 per cent. bromine to 33 per cent. of potassium), should pass through the animal body without exerting any effect.

EFFECT OF POTASSIUM BROMIDE UPON THE ORGANISM.

Potassium bromide has none of the irritant effects of free bromine upon the animal tissues; potassium bromide solutions are very rapidly absorbed by all of the mucous membranes, and that probably in an undecomposed condition—for there are no evidences to be found upon the mouth, pharynx and stomach of a setting free of the bromine. Besides this, according to Binz, the potassium bromide is decomposed by acids with much more difficulty than the similar iodine combination. According to Bill, this salt, when it comes in contact with the *sodium chloride* of the body, forms potassium chloride, which appears in much larger quantity in the urine, while the sodium bromide is retained in the body for some time. Whether the

bromine alone is temporarily in free condition in the blood and tissues, is not positive but probable. The bromine combined with an alkali appears again in the urine and saliva. According to Voisin, Bowditsch and others, the bromine salts are excreted by the mammary glands, almost all of the mucous membranes and the skin, on the surface of which they undergo decomposition (whence the cough, conjunctivitis, and eruption on the skin). The excretion begins one quarter of an hour after the administration of the drug, and lasts for two to three weeks (M. Rosenthal). The daily administration of bromine, therefore, results in cumulative effects. We have never been able to confirm the statement that bromine imparts a special odor to the breath.

LOCAL EFFECTS UPON THE SKIN AND MUCOUS MEMBRANES.

It does not affect, nor does it undergo absorption through the unbroken skin. Injected in concentrated solution under the skin or into the urethra, it causes severe pain and inflammation.

A bromine salt is excreted upon the skin with the perspiration (Guttmann); possibly owing to the bromine thus set free, we sometimes even after a few concentrated doses have an acniform eruption appear over the whole skin, especially over the face and breast, due to an inflammation of the glands of the skin and hypertrophy of the papillæ; this eruption is sometimes in the form of erethema nodosum, which may degenerate into foul smelling ulcers that are healed with difficulty, and sometimes in the form of an urticaria or eczema.

The administration of strongly diluted doses, and in this way the drug should always be administered, is followed by no further local effects, apart from the salty taste, than a sensation of warmth in the stomach. Gastric catarrh or disturbances of appetite rarely occur, even after long continued use of the drug. When given in greater concentration there is severe burning in the mouth and epigastrium, eructation, as well as vomiting, and diarrhœa. When administered upon an empty stomach these effects are more marked, and are to be considered as the effect of the local inflammation and irritation of the mucous membranes.

The increased excretion of saliva, which is one of the earliest effects of the drug, is reflex, and due to the irritation of the mucous membrane by the sharp tasting substance. Later on a *diminution in the* salivary secretion and dryness of the pharynx

set in. The mucous membrane of the mouth, pharynx and larynx sometimes becomes pale, sometimes reddened, and in individual cases it has even been found œdematous (hoarseness).

GENERAL EFFECTS.

Brain.—Shortly after the administration of medium doses (5.0—10.0 grms.) there set in frontal headache and a dull feeling of pressure, as if the contents of the cranium were being pressed together; the sensorium is benumbed, and clearness of thought is affected, just as in other forms of headache. The headache soon passes away, but the psychical disturbances remain for the rest of the day. Further cerebral symptoms are: impaired memory, incapacity for clear and logical thought, and a difficulty in finding the proper words to express oneself. Speech is difficult, slow and dragging and there is loss of power over the nerves of the organs of speech.

A tired and relaxed feeling is the result of even small doses. The nervous irritability, which is the effect of mental overwork, can be soothed and an agreeable sense of rest can be produced by even small doses of potassium bromide (3.0 grms.).

Some observers affirm and others deny that this drug is a hypnotic. Our experience, based upon the observation of patients, agrees with that of Krosz, who describes the action of the potassium bromide upon the brain in the following manner: "It does not produce a forced sleep, as the narcotics like morphine, for example, do, but rather a peculiar feeling of rest, which invites sleep; an indifference to external impressions, a diminution in the reflex irritability of the brain, so that events which would ordinarily give rise to excitement are now looked upon with indifference."

Bodily exercise, bathing, eating and drinking will counteract the effect of potassium bromide upon the heart and temperature, but do not remove the feeling of weariness.

The many contradictions to the above observations depend, we are convinced, upon the doses which have been administered being too small to produce the effects.

All of these cerebral symptoms are the effect of the bromine, for they can be produced also by the sodium bromide, while they do not follow the administration of the potassium chloride. Whether they are the result of a direct affection of the cells of *the brain* by the bromine, or of a change in the circulation *(anæmia) of* the brain, we do not know. According to *Sokolowski, there* is in trephined animals, after the administration

of bromides, a narrowing of the cerebral bloodvessels. This is a fact, however, which needs confirmation.

Spinal Cord, Reflex Irritability and Sensibility.—Medium doses of from 5.0–10.0 grms. produce in adults the following symptoms; 1. The irritability of the mucous membrane at the edge of the gums, base of the tongue, surface of the epiglottis, pharynx and fauces is diminished or even entirely abolished, so that tickling of these structures does not produce cough or the movements of vomiting. Contradictory observations seem to depend upon the smallness of the dose. We ourselves have found that in removing laryngeal polypi no further preparation of the patient is necessary than the administration of the potassium bromide. 2. When the dose is increased to 15.0 grms. the remaining mucous membranes, such as the urethra, vagina, conjunctiva and even cornea become entirely insensitive. 3. So also very large doses produce insensibility of the skin, both to tickling and to painful sensations (pricking and burning).

Experiments upon animals have taught us that these psychical effects and interference in reflex action are dependent upon a disturbance in the connection between the sensitive nerves of the brain (n. opticus, acusticus) and medulla oblongata on the one hand and the motor elements and psychical centers of the cerebral hemispheres on the other (Krosz, Eulenburg, Guttmann). For this cessation of reflex action and sensibility occurs even in the extremities of a frog from which the circulation has been cut off, so that the potassium bromide cannot have affected the limb through this channel. Furthermore, the tetanoid spasms produced by strychnine can be counteracted almost entirely by potassium bromide (Schroff, jun.).

In frogs, however, according to Krosz, even after complete paralysis of all reflex action, voluntary motion is still possible when even the strongest irritation does not produce a reflex movement; mere passive stretching of the limb of the animal will immediately result in its retraction.

Peripheral sensitive and motor nerves suffer paralysis to a less degree and later than the nerve centers. So that the paralytic effect of this drug upon the nerve centers extends from the center to the periphery.

Although voluntary muscles, when placed in a solution of potassium bromide are soon paralyzed, yet while in the body enormous doses are necessary to produce this effect. Ordinary medicinal doses produce only very slight muscular weakness.

The respiration, both in cold and warm-blooded animals,

and also in human beings, under the influence of this drug, becomes slower and is finally brought to a standstill (by fatal doses). The symptoms of dyspnœa, such as difficult respiration, cyanosis, and protrusion of the eye-balls, which occur in warm-blooded animals, after poisoning with very large doses, are due to the weakness of the heart, insufficient circulation, and consecutive carbonic acid poisoning.

Circulation and Temperature.—Large doses produce in men and the larger animals a weakening and slowing of the heart's action.

Krosz observed, after a dose of 15.0 grms., a diminution in the frequency of the pulse by almost half the number of beats; often also an irregularity in the rhythm of, and an intermittence in the pulse. Even when smaller doses, such as 5.0 grms., are administered for a long time in epilepsy, we have observed with certainty an extraordinary weakness of the heart's action, which often necessitated the suspension of the remedy.

The maximum of the changes in the circulation, and the diminution in the temperature is attained, in from 2–6 hours after the administration of the remedy. The temperature falls after large doses, both in men and animals. 10.0 grms. cause a fall of from 0.5°–0.8°C. 15.0 grms., about 1.2°C (Krosz). For this reason potassium bromide is the best drug to use for sleeplessness and restlessness in febrile diseases (Senator).

Experiments upon animals have shown that the effects upon the heart, are not dependent upon an irritation of the inhibitory nerves of the heart, but, as in potassium, to a paralyzing action upon the heart muscle and nerves. When fatal doses have brought the heart to a stand-still in diastole, even the strongest local irritation will not cause the heart to contract again. How much of the decline in blood pressure is to be accounted for by a paralysis of the vaso-motor centers, and the vasor muscles, and how much is due to weakness of the heart, is unknown.

Organs of Generation.—Various observers (Voisin) have noticed a diminution or an entire abolition in the sexual desire in consequence of the drowsiness and sensory disturbances. The menses, if formerly scant, become more plentiful and last longer (M. Rosenthal).

Dysmenorrhœa disappears, probably owing to the diminished blood pressure, and weakening of the reflex nervous influence emanating from the uterus and ovaries.

We have various, and somewhat contradictory assertions

concerning the urinary excretion. According to some, there is pain in the region of the kidneys, and increased excretion of urine, while others believe that the drug diminishes the latter. Some describe the urine as of normal composition, others assert that it is more strongly acid.

Chronic Potassium Bromide Poisoning.—All of the above mentioned changes in the brain and spinal cord, the circulation, and organs of respiration, and the skin, are also seen as the result of chronic poisoning. In the latter case, however, we have also bronchial catarrh, with dyspnœa and attacks of coughing resembling those of whooping cough, disturbances of nutrition (want of appetite, great thirst, and diarrhœa), anæmia and wasting.

Death from Potassium Bromide.—The order in which different organs are paralyzed, by a single fatal dose of potassium bromide, varies with the method of administration. If the potassium bromide be injected directly into the blood, the heart is first paralyzed. But if absorbed from the stomach, the central nervous system is first affected, and the heart afterwards. Death, however, is always due to paralysis of the heart.

In chronic poisoning death may set in through the development of a pneumonic process in the lungs, or of an intestinal catarrh, with very severe typhoid or choleriform symptoms.

THERAPEUTIC APPLICATION.

Potassium bromide is at present very widely used, especially in many of the diseases of the nervous system.

It is most used in epilepsy, and to-day there is perhaps not a single epileptic who has not taken the remedy. We base our conclusions as to the utility of the potassium bromide in epilepsy, upon our own numerous observations, already spoken of elsewhere ("*Ueber Epilepsie*"), and the reported experience of others. Potassium bromide is in no way an infallible and sovereign anti-epileptic remedy, but it is certainly better than any other that we possess. A small number of cases are cured, another set of cases remains unaffected, while a third series, and that is the most numerous, is more or less permanently improved.

Although some authors do not recognize, or at least have never themselves seen, any cases that have been cured (to the latter class we ourselves belong), yet the positive assertions of other reliable observers do not admit of absolute contradiction. But we must remember that many of the so-called cures have

been reported after a short period of freedom from attacks. On one point however all observers are agreed, namely, that potassium bromide makes the intervals between the attacks longer, sometimes even many months in duration, and that when the attacks do occur after this lengthened interval, they are neither more violent nor more numerous than usual. Even this result is of extraordinary value, when we consider how frequently other remedies and methods of treatment fail, and assures to bromide of potassium its position in the therapy of epilepsy.

The attacks often cease at the very beginning of the treatment, which is scarcely ever the case under the use of other remedies; but if the remedy be suspended, the attacks recur. Particularly remarkable, however, is the positive assertion of many observers, that very often the drug produces, at the same time, a great improvement in the psychical disturbances of epileptics, so that the patient may recover even from a condition of dementia. Other observers, however, have not been able to confirm these views.

We must repeat, however, that sometimes the drug is entirely inoperative; this we can know from our own experience.

At first it was supposed, that in certain forms of epilepsy, whether distinguished by ætiological or symptomatological data, were more influenced by potassium bromide than other forms. But the more extended our experience, the less is such a view confirmed. Œtiology, duration of the disease (up to a moderate limit), frequency, character, and number of the attacks, appear to have no influence in determining the efficacy or non-efficacy of the potassium bromide.

We should emphasize the fact, however, that the drug is potent only in real epilepsy, and not in symptomatic epileptiform attacks. Considerable attention should be given to the method of administration of the drug. Almost all observers agree upon two points: 1st, that the remedy should be given for a long time; and 2d, that it must be given in large doses. In adults we should begin with 5.0 grms., and increase to 10.0 and 15.0, and where there is great tolerance, even 20.0 grms. per day. The remedy must be suspended or diminished when pathological effects begin to appear (such as digestive disturbances, diarrhœa, acne, and furuncles, general muscular and heart weakness). The ordinary dietetic observances (such as *non-use of* spirituous liquors, coffee, etc.), which are ordinarily *insisted upon* in the treatment of epilepsy, should not be *neglected here.*

Some observers have found that, when the potassium bromide alone was without effect, or almost so, a combination of the drug with other remedies, such as zinc oxide, conium, chloral, *et al.*, was often effective.

We ourselves have had experience only with the combination recommended by Clouston for psychical affections, that is the potassium bromide with Indian hemp, but have not found it any more effective than the simple potassium bromide.

As we might expect, potassium bromide has been used in a large variety of other nervous diseases, mostly in the so-called functional neuroses. Concerning its use in some of these we have an extended experience, so that we can express an opinion. It does not seem to be without good effect in the eclamptic attacks of small children, although in this condition it often happens that the convulsions cease without any remedy. Concerning its use in chorea the results are too contradictory to enable us to arrive at any positive conclusion. Potassium bromide is often used to relieve some symptoms of hysteria (such as sleeplessness, hyperæsthesia, neuralgia, hystero-epileptic convulsions, &c.). We are, however, decidedly of the opinion, that the treatment of hysteria and its prominent symptoms should be a psychical one, and that the administration of drugs should be avoided as far as possible. We therefore consider the administration of this drug as unnecessary in this condition and even injurious; although we do not deny that it temporarily relieves the above named symptoms. In tetanus it has been used, acording to some observers, with good effect. We have not been able to convince ourselves of its utility in this affection, but should recommend its trial in large doses. Few, however, will dare to trust to potassium bromide alone, without chloral or curare, in this affection and it therefore will be difficult to obtain any data from which to estimate its value.

Potassium bromide has an excellent effect in conditions of increased general irritability, fibrillary contractions, nervousness, and sleeplessness, which occurs in anæmic and debilitated persons, as well as in those who have suffered from some painful disease. Especially useful is it, however, when these conditions are the result of immoderate mental exertion and excitement. It acts by producing a condition of rest of the nervous system, and after its use has been continued for some time, healthful sleep. Whether the drug acts as a real hypnotic, and has the power to compel sleep in pathological conditions, is uncertain. Our experience concerning this point is negative. In

patients suffering from mental diseases it is sometimes given as a hypnotic and may produce sleep, after chloral and morphine have both been ineffective.

Sometimes it is also used for the methodical treatment of these affections. Apart from its application in the mental derangements of epileptics, the indications for its use in these diseases are the same as those for the similar use of morphine in cases of insanity (Compare morphine.) In delirium tremens chloral should be decidedly preferred.

A number of recommendations for the use of potassium bromide in other affections we do not mention at all, because the majority of these have not been confirmed. But we must not forget to mention its local application in the production of anæsthesia of the soft palate, pharynx and larynx. By painting locally with concentrated solutions or by giving large doses internally (10.0) there is produced a diminished reflex irritability, which is very important for the performance of operations and examinations with the laryngoscope.

It is also useful, when applied locally in concentrated solutions to the pharynx, to check the vomiting, which sometimes accompanies the cough of phthisis. Very recently Friedreich reports the excellence of the remedy in hyperemesis. The inhalation of a 2–5 % solution has been very much praised in the paroxysms of coughing which occur in tussis convulsiva, while its internal use in this affection is entirely iueffective. Joffroy recommends the drug in the spasm of the glottis, which sometimes occurs in tracheotomized children, when the canula is to be removed. This spasm of the glottis may be prevented when KBr. is administered to the children for a few days previous to the removal of the tube (children of 4 years 2.0 grms. daily.)

Dosage.—If potassium bromide is to produce any effect, it should be given in large doses. 1.0–2.0 pro dosi. In epilepsy up to 5.0 grms. pro dosi three times a day, so that the daily quantity should amount to 15.0–20.0 grms. In solution or in powder. In children 0.1–0.5. It should be given during eating, since in this manner the local effects upon the stomach are diminished, while the general effects are as strong as when given upon an empty stomach. Milk can be administered between the individual doses. For painting the pharynx, a solution in water or glycerine of the strength of 1 to 1 or 1 to 2 should be used.

3. SODIUM BROMIDE—SODIUM BROMATUM.

Sodium bromide has a much less disagreeable taste than the potassium *bromide; it is* deliquescent and easily soluble.

ACTION AND APPLICATION.

Those authors, who consider that the potassium bromide exerts effects only similar to those of potassium, believe that the sodium bromide is a no more active agent than the sodium chloride, and therefore class this drug among the indifferent remedies.

But this is not really the case. Several physicians have noticed similar poisonous effects from the use of sodium bromide as from the potassium bromide, such as eruptions on the skin, benumbing of the power of sensation, difficulty of speech, etc. Stark and Hallis observed the same curative effect in epilepsy. Furthermore comparative observations upon the effect of the potassium chloride and sodium bromide upon healthy men and epileptics, have shown the utility of the latter drug and the uselessness of the former in epileptic attacks, while the sodium bromide in healthy men produced the ordinary bromide cerebral effects, such as weariness and drowsiness, together with diminution of reflex irritability.

We ourselves (Rossbach) have been able to diminish or even suspend the reflex irritability of the pharynx, and laryngeal mucous membrane both in epileptics and in cases which were about to undergo laryngeal operations, by the use of the sodium bromide just as well as by the use of the potassium salt.

We found a cessation of the attacks and an improvement in the health of epileptics together with a suspension of the irritability of the pharynx and larynx under its use. When, after the long continued use of potassium bromide solutions of the proper concentration we were compelled to suspend the remedy on account of the appearance of great weakness of the heart, we have substituted in its place the sodium bromide, with the same therapeutic results. Indeed, we now administer instead of the potassium bromide, the sodium salt from the very beginning. M. Rosenthal is of the same opinion as we are. In children the sodium bromide should be preferred.

The dosage and administration is similar to that of potassium bromide. On account of its ready deliquescence, it should be ordered in solution, or if in substance, it should be kept in glass vials.

Ammonium bromatum is entirely superfluous; its application and dosage are the same as above. *Zincum bromatum*, recommended by Hammond in hysteria in from 0.1–0.4 pro dosi. *Chininum hydrobromicum*, easily soluble in water and glycerine, recommended in doses of 0.1 about five times a day, for the vomiting of hysterical and pregnant women and in various neuroses of the stomach. Monobromide of camphor, *Camphora monobromata* $C_{10}H_{15}BrO$, that is camphor, in which one atom of hydrogen has been

replaced by one atom of bromine. It forms white crystalline masses, readily soluble in alcohol and ether and with difficulty soluble in water. According to Bourneville and Lawson this preparation has a depressing effect upon the action of the heart, respiration, and temperature, both of men and animals. In addition to this it produces clonic contractions of the feet, drowsiness and after long continued use, a general wasting of the body. It has been recommended as a hypnotic and against all possible neuroses and neuralgias, and generally for uses similar to that of KBr. (Compare this.) Berger has only found it of use in nervous palpitation of the heart and conditions of irritation of the genito-urinary organs.

THE IODINE COMPOUNDS.

I.—IODINE—IODUM.

Iodine, like bromine, is found in combination with metals, often in conjunction with chlorine, in sea water, sea plants and salt springs.

It presents large, soft rhombic crystals, blackish gray in color, and having a metallic lustre. Its vapor, which is given off even at ordinary temperatures, is of an intensely violet color, which turns to a deep blue under the influence of a higher temperature. It is with great difficulty soluble in water, more easily in alcohol (giving us the tincture), very readily in ether (brown colored solution), chloroform, and bisulphide of carbon (rose-colored solution).

Even watery solutions of potassium iodide and sodium iodide (4 per cent.) can dissolve considerable quantities (3 per cent,) of iodine, producing a brownish colored solution (Lugol's solution). This solution is used when we have need of a watery solution of iodine. But we do not obtain in this preparation a simple solution of the iodine, but a real chemical combination (biniodide of potassium KI_2), which is, however, very unstable.

Iodine is chemically very similar to bromine and chlorine, only less powerful so that it can be liberated by the latter elements from its combinations.

PHYSIOLOGICAL ACTION.

For reasons to be given later on, it is necessary to distinguish between the action of free iodine and of that of its salts, especially the potassium and sodium iodide. We must not forget, also, that free iodine, when applied therapeutically, or in experiments on animals, is generally used in the form of the tincture, in which the alcohol necessarily exerts some effect. We shall here speak only of the effect of the iodine. We must, therefore, exercise great discrimination in making use of the older observations.

Action Upon the Basement Substance of the Tissues.—The effect of iodine like that of bromine and chlorine, upon the animal tissues, is dependent upon its relationship to hydrogen, and consists in the formation of the iodide of hydrogen and the destruction of the molecular structure. This effect is not so violent, however, as that of bromine and chlorine.

The relationship of iodine to albumen has lately been the subject of thorough investigation. It was long ago thought that the loss of the blue color of iodide of starch solutions upon the addition of albumen, and the decolorization of the iodine in solutions of albumen, were due to the formation of an albuminate of iodine. Boehm–Berg found that this combination of iodine and albumen was a very loose one, and that it could be decomposed both by coagulation of the albumen, and by dialysis. The alkali of the albumen, in natural albuminous solutions, is not saturated by the free iodine which has been added. But neutral solutions of albumen, as well as those free from salts, immediately turn acid upon the addition of the hydrogen iodide. When the albuminate of iodine is decomposed, either by coagulation or dialysis, the alkali that is set free from the albumen combines with the iodine to form compounds of iodic acid and hydriodic acid. Whether a similar change takes place in the living body is unknown.

Hæmoglobin, also, is capable of combining with large quantities of iodine, without losing its properties. Lime solutions can also absorb considerable iodine.

Action of Iodine Upon the Different Organs.—Upon the skin the tincture of iodine, after repeated painting, produces a sharp, prickling sensation, inflammation of the skin, with an emigration of white blood corpuscles (Volkmann). It does not produce a very deep effect—iodine in substance, however, is capable of forming an eschar. Soon the epidermis peels off in larger or smaller pieces, of a characteristic yellow or yellowish brown color. A part of the iodine thus painted on is vaporized, and may be inhaled, while another portion volatilizes with the alcohol, (perhaps is temporarily converted into iodine ether or iodoform,) and may be absorbed through the unbroken skin (Röhrig).

The mucous membranes, also, when brought in contact with vaporized iodine, or iodine painted upon them, become inflamed—conjunctivitis may thus be caused; there is an odor resembling that of hydrochloric acid; catarrh of the nose and frontal headache; inflammation of the larynx and bronchial mucous membrane, with severe cough and pain in the chest. In the digestive canal iodine produces a nauseous and extremely saline taste, an increased flow of saliva, pharyngitis, and according to the size of the dose, nausea, vomiting, severe gastric pains and diarrhœa; finally, in very large doses, a toxic gastro-enteritis, with its further consequences.

Since iodine coagulates the secretions of suppurating sur-

faces, it acts in a manner similar to lead and nitrate of silver solutions, enabling the sore to heal more rapidly underneath the coagulum.

When administered internally in strongly diluted medicinal doses, for a longer or shorter time, free iodine, either in the form of the tincture or the potassium biniodide, remains free only for a very short time. This short period is sufficient to produce the severe effects upon the respiratory and digestive mucous membranes which we have described above, and which under the internal use of potassium iodide do not exist, or occur only after a long time. The free iodine cannot be shown to be present either in the stomach, blood, or secretions as such, but is always present in the form of sodium iodide or sodium hydriodide, or in combination with albuminoid bodies. We cannot, therefore, speak of a general iodine effect from iodine given internally in some free form, or applied as an ointment. In either case the effect would be identical to that of potassium iodide and sodium iodide, and can, therefore, be best discussed together with these preparations.

We must, however, give special consideration to the action of iodine when injected directly into the tissues and cavities of the body. For when thus applied it produces an entirely different effect from that of similar injections of potassium and sodium iodide. At the present time iodine injections are used much more frequently than formerly in the treatment of hypertrophied lymphatic glands, ovarian cysts, echinococci cysts, hydroceles, hydrarthoses, diseases of the pleural cavities, etc., and about 35 cases of death after injection of iodine in human subjects have been reported, the greater part of which were due to the carelessness in the injection of the iodine. But a single one of these cases—that of Rose—was accurately observed, and even this one is not well fitted for the study of the physiological action of iodine, since the preparation used was a mixture of the tincture and potassium iodide. A mixture of the tincture of iodine, aqua destillata āā 150.0 grms. kal. iodid. 4.0 grms., was injected into the ovarian cyst of an otherwise healthy girl 16 years of age, who, although chloroformed, became conscious before the injection was completed. Pain was so severe as to cause fainting; a part of the solution came out again after the lapse of about an hour. The amount of free iodine injected was 15.0 grms., of which 7.0 grms. may have flowed out again, so that 8.0 grms. of free iodine remained in the body. The effect produced was not entirely due to the iodine, but partly

to the chloroform and partly to the alcohol in the tincture, and also the K I. Apart from these, and the terrible pain which it caused, owing to the circumstances just stated, the operation itself had some influence in the result. But none of these causes explain the fatal result which suddenly took place nine days later. We cannot believe that it was due to the iodine, since Boinet states that he has injected as much as 200 grms. of the pure tincture of iodine into ovarian cysts without harm. We shall not, therefore, go any further into the above case, but will base our remarks upon the experiments of Böhm upon animals. He injected iodine, in the shape of the sodium biniodide solution, directly into the blood of dogs; and since there was no alcohol present, the effects which were observed can not have been due to any thing but the iodine. The following are the results of these experiments:

Dogs can bear the injection of 0.02–0.03 grms. of free iodine for every kilogram of bodily weight (dissolved in 2–3 parts of sodium iodide) directly into the blood, without any disturbance in health resulting. This quantity calculated for a man 70 kilograms in weight would be 1.4–2.1 grms. of free iodine, which ought to produce no disturbances when injected directly into the blood. Dogs, in whom 0.04 grms. of free iodine pro kilo were injected, died, with the same symptoms, and in the same length of time as those into whose blood fatal quantities of sodium iodide were injected.

The injection itself is only followed immediately by dangerous symptoms when large quantities have been injected, which by coagulation of the blood cause rapid death.

In all other cases, animals show few signs of pain while the injection is being made, and immediately after the operation run about as lively as ever. After the lapse of 4–6 hours, however, general weakness and disturbed respiration begin, which after 12–24 hours more may lead to convulsions and death.

Observations upon men and animals agree in the fact, that large doses do not produce functional disturbances of the cerebrum and spinal cord as bromine does. But the influence of this drug upon the organs of circulation is not the same in men and animals, as far as observation has shown. Rose asserts that in human subjects there is produced in the beginning an arterial spasm which may even lead to occlusion of the larger arteries (disappearance of the arterial pulse in the periphery, with pale and cold skin lasting for several days, although the *force and rapidity* of the heart's action are increased!) Finally,

however, there is generally paresis of the peripheral arterial system, the pulse reappears and the skin becomes very red. Böhm found nothing of this kind in animals. We do not, therefore, believe that the above mentioned arterial spasm is dependent upon the iodine.

In the blood of animals free iodine decomposes even in the active circulation considerable quantities of coloring matter. This is shown by the presence of this coloring matter in effused blood serum pleuritic exudations, as well as in the urine.

An almost constant effect of iodine poisoning in animals is the appearance of pleuritic exudation of a blood color, (simple sodium iodide poisoning produces a clear light yellow exudation) and œdema of the lungs. The urine is also bloody in color owing to the presence of blood corpuscles, which later on form themselves into beautiful cylinders, and in some places are covered with epithelial cells. We also find the urinary tubules of the cortex filled with blood corpuscles and detritus.

In the case of the girl, reported by Rose, there appeared an eruption on the skin ; there was also great thirst, severe vomiting of masses of matter containing considerable iodine, and a great diminution in the excretion of urine. The urine during the first eight days contained no albumen or blood. Post mortem examination showed that the kidneys were normal. The large percentage of iodine contained in the urine at first, rapidly diminished, but returned again on the seventh day to a medium percentage. The excretion of saliva was diminished from the very beginning, but the salivary glands became very much swollen. Post mortem iodine was found in the whole of the intestinal tract and the lungs. No iodine was found in the bladder, skin of the abdomen, brain, and spinal cord. Since no trace of iodine was to be found in the blood serum, Rose concluded that it had been contained in the blood corpuscles.

All of the experimenters upon animals contradict the assertion of Rose that iodine is excreted by the gastric mucous membrane. They assert that the gastric mucous membrane is always free from iodine ; most of the iodine is excreted by the kidneys.

Therapeutic Application.—On account of the poisonous action of iodine upon vegetable parasitic growths, a weak tincture of iodine or Lugol's solution may be used in the affections of the skin and mucous membranes, depending upon these spores such as chloasma, soor, etc. Rossbach has seen iodine inhalations cure an otherwise incurable pneumomycosis aspergillina. Tincture of iodine given internally is sometimes ef-

fective in stopping vomiting. An explanation of its action in these cases is as difficult as it is to define the cases in which it can be given with an expectation of good results. Our own experience has taught us that it is most apt to be useful in the so-called sympathetic or nervous vomiting. Vomiting due to cerebral causes is not affected by it. So it may be used in the vomiting of pregnancy when other means have failed. But even in these cases it has more frequently failed than benefited.

Tincture of iodine is very much used externally. First of all for injecting into pathological sacs, cavities and swellings, in the walls of which it is desired to excite an adhesive inflammation which is to obliterate these spaces. A large experience has shown that iodine is the best of all the means used for this purpose. Lugol's solution is better than the tincture because less irritating. Above all the best results are attained by such iodine injections in hydroceles. In pleurisy, also, with purulent effusion, the tapping and emptying of the pleural sac may be followed, after some time, by iodine injections.

Our experience in the analogous treatment of purulent peritoneal exudations is unsatisfactory. Iodine injections seem however directly contra-indicated in purulent inflammations of the joints, since a relatively large number of fatal cases have been observed after their use. So, also, in ovarian cysts the iodine injections have been condemned; for, in the first place, they can only be used in simple cysts, and, secondly, their use has been known to be followed by fatal suppuration and peritonitis. Better results have followed from this method of treatment in echinococci of the liver and in hydronephrosis; in the former especially, we have a number of favorable cases following from the injection of iodine solutions. These injections are very rarely used in solid tumors; although recently used by Lücke and others in struma. The best results are obtained in goitres, due to a simple hypertrophy of the thyroid gland.

Iodine is very much used for external purposes, either as a paint or ointment. Of these the tincture appears to be the most useful, while the ointment is of little use. The conditions in which iodine may be thus used are mostly acute or subacute inflammatory processes affecting superficial organs, thus in joint inflammations, inflammations of the lymphatic glands, periostitis, pleuritis, etc. Its utility in these cases we believe to depend entirely upon the fact that it produces an irritation *of the skin*; experience teaches that tincture of iodine is not

entirely useless but in most of these cases, with the exception, perhaps of inflamed lymphatic glands, the vesicants should be preferred. Tincture of iodine is also used where we wish to cause an absorption of inflammatory products, in conditions similar to those just mentioned. In hygromata, ganglion, etc., tincture of iodine may be used with some benefit. As an injection in blenorrhœa of the mucous membranes or for indolent fistulous tracts or as a wash for various ulcerating diseases of the skin there is no better remedy.

Dosage and Preparations,--Iodine itself is very rarely used externally, either dissolved in oil, bitter almond oil or glycerine (1 to 3 or 5).

2. Tinctura Iodi of a brownish-red color 1 to 10 Spiritus (10% solution), internally from 3–10 drops (ad. 0. 3 pro dosi ; ad. 1.0 pro die) ; to be taken in a mucilaginous vehicle. Principally used as an external application. If it is to be used for some time, and a strong inflammation of the skin is to be prevented, it should be combined with equal parts of Tinct. Gallarum.

3. Tinctura Iodi decolorata, 10 parts of iodine, sod. sub sulph. and aqua destillata, 16 parts of liq. ammon. caust. spir. and 75 parts of spirits. To be applied externally.

4. Lugol's solution of iodine, 1.0 of iodine, and 2–0 of pot. iodide in 30 of water. For external application, especially for injections (diluted).

2. POTASSIUM IODIDE.—POTASSIUM IODATUM.

Potassium iodide, KI, is found in seawater, etc., always associated with potassium bromide. It forms large colorless almost opaque cubes, which are soluble in 0.7 parts of water at ordinary temperature, and in 40 parts of absolute alcohol. The solution is either neutral or slightly alkaline. The watery solution of potassium iodide can dissolve large quantities of iodine.

PHYSIOLOGICAL ACTION.

It is generally acknowledged that a large part of the effect of the potassium iodide is due to its iodine component and that only in relatively very large doses does the potassium also produce noteworthy effects upon the animal body. Even those investigators who believe that the effect of the potassium bromide does not in any way depend upon the bromine, hold the above view concerning the potassium iodide.

Effect of the potassium iodide upon the organism.—We do not yet know how to explain the iodine effect from the use of the potassium iodide. The question is, whether free iodine is set free from its combination with potassium in the body. It does not seem that this ever takes place in the stomach, for when potassium iodide is injected into the stomach of living animals, it is impossible, after a short or long period of time, to get any

of the reactions of starch and free iodine in the stomach (Pelikan). It is, therefore, supposed that in the presence of the sodium chloride the salt is decomposed, giving rise to the formation of potassium chloride and sodium iodide, under which form the iodine reappears in the urine; or it may be that iodine is set free in the stomach, only immediately to be again converted into a hydriodic acid salt or an iodine albuminate. So that we can never obtain the reaction of free iodine in the stomach.

We can not directly prove that even a temporary liberation of the iodine from its salts takes place in the blood and tissues. But observation outside of the body would lead us to this conclusion. This view is also supported by the facts shown by Liebreich and Issersohn, that after the subcutaneous injection of potassium iodide first iodine and potassium were excreted, and later on the alkali alone; this could only occur if a decomposition of the salt had taken place. Binz found that free iodine was separated from watery solutions of potassium iodide in the presence of protoplasm and carbonic acid. He also found, with Kämmerer, that the same thing occurred under the influence of carbonic acid and oxygen, by the passage of the oxygen, according to Buchheim, from one body to the other. This free iodine then must enter into immediate combination with the albuminoid bodies of the blood, lymphatic glands, or walls of vessels. The various hypotheses as to the influence thus exerted upon the albuminous bodies, and the many explanations of the general iodine action, which have for their basis this iodine combination with the albuminoids, are not very well founded, and we shall therefore only give them a short consideration:

1. The combination of the iodine atoms with the albuminoid molecules causes the latter to undergo decomposition more readily, and thus a more rapid interchange of materials takes place in the body, and a wasting of tissues sets in (Kämmerer).

2. The lead and mercury albuminates when present in the organism, are thus more rapidly excreted and taken out of their organic combination by the administration of the potassium iodide (these assertions of Melsen, which were doubted by F. C. Schneider, have recently again been confirmed by Annuschat.

3. Septic materials circulating in the blood are destroyed in this manner (Kämmerer).

4. The influence of free iodine upon the albuminoid bodies of the walls of the vessels causes the drug to act as an irritant,

and thus promote absorptions through the walls of the vessels (Buchheim).

5. All the tissues have not the power of separating the iodine from the sodium and potassium iodide, thus the brain has not this power, gummatous tumors of the brain have however (Binz). In this way we can explain the varying strength of the iodine action upon the different organs.

Potassium iodide, like free iodine* administered medicinally, appears very rapidly in all of the secretions and excretions (saliva, urine, bile and milk) a few minutes after its absorption. In the course of 24 hours almost all of the iodine has again been separated from the body, chiefly under the form of a sodium combination (Bachrach).

This is certainly in favor of the theory expressed above, namely that iodine, even if it be set free in the organism, does not remain so long, but rapidly satisfies its affinities by combination with hydrogen and the alkaline metals; and furthermore that the iodine albuminates formed in the organism do not remain under this form for any length of time.

The iodine salts excreted in the saliva, in the mucus of the air passages, and on the surface of the skin with the perspiration, may be decomposed under the influence of the ozone, etc., so that free iodine may appear in these situations (Buchheim, Sartisson).

The largest portion of the potassium iodide is absorbed by the kidneys, salivary glands and lungs, and perhaps also by the testicles. Smaller quantities by the liver, spleen, lymphatic glands and muscles, least of all by the pancreas; none at all by the brain (Heubel). Sartisson, from whom these estimates are taken, found that the salivary glands, while in the living body, have a greater affinity for potassium iodide than when outside of the body; furthermore, that they absorb less potassium iodide after section of the nerves which supply them than do others with uninjured nerves. The minute quantities found in the brain (0.003%) may have been due to the blood contained in the brain.

Effect upon the skin and mucous membranes.—Potassium iodide has no irritant or caustic effect upon the unbroken skin and is not absorbed through it. If all of the mucous membranes be protected from the water by a coating of fat, and the prepuce be covered by a rubber cap, while the air which is breathed by the subject under experiment, is brought to his mouth from

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* Compare pp. 279 and 282.

without, the body may be bathed in potasssum iodide baths for hours without any trace of iodine appearing in the urine. If an iodine salt was found in the urine, after one of these baths, it was due to absorption through some uncovered mucous membrane, or to inhalation of the vapor of iodine with the air. The potassium iodide salts also only lead to the absorption of iodine when they are decomposed by the fatty acids of the skin (Röhrig).

The iodine salt which is excreted upon the skin with the perspiration, is decomposed by the fatty acids of the skin, and the iodine thus set free produces a roseolar eruption, either pustular, papular, or erythematous in character. If great cleanliness, by means of daily baths, be observed, this eruption will disappear or perhaps be entirely prevented.

Potassium iodide is absorbed into the blood by all of the mucous membranes.

Even comparatively large doses of potassium iodide (1.0–3.0 grms.), administered for weeks and months by the stomach, are not followed in adults by any disturbances of the mucous membranes of the digestive passages; there is only a sharp saline taste and thirst. We observed 17 cases in which large doses of pure potassium iodide (1.0–3.0 grms.) were administered three times a day, 1–2 months, for struma, and not even in a single case did we observe the least diminution of appetite or disturbance of digestion. The gastric disturbances that have hitherto been observed, have resulted from the use of the tincture of iodine, or potassium biniodide, or free iodine, or potassium iodide rendered impure by admixture with free iodine or iodic acid (HIO_3) (Melsens). Free iodine, as we have already mentioned, produces local symptoms of irritation. Buchheim also has asserted that potassium iodide may be administered for years without influencing the general nutrition in the least. Furthermore Gilbert asserts that in an experience of twenty-five years he has never seen the long-continued use of potassium iodide followed by gastro-enteritic symptoms, although tincture of iodine and solutions of potassiun biniodide do produce gastro-enteritis very readily. It is, therefore, decidedly wrong to give any other preparation internally than the sodium or potassium iodide. The internal administration of potassium iodide, however, renders the external application of free iodine, as for example the tincture of iodine, superfluous, except for injecting into cystic tumors and similar affections.

Entirely different, however, is the effect of potassium iodide

upon the conjunctiva, mucous membrane of the nose, mouth, pharynx and œsophagus, all of which under the continued use of potassium iodide become characteristically inflamed. We can distinguish an iodine conjunctivitis with severe lachrymation which sets in in the very beginning (Ricord), or after months of treatment (P. Bernhard); a nasal catarrh, accompanied by severe frontal headache, and the excretion of a thin mucus from the nose, which gives rise to an intense iodine odor; also an iodine angina and an iodine salivation, the latter, however, being unaccompanied by any foul odor from the mouth, and running its course without any symptoms of stomatitis or gingivitis, or swelling of the salivary glands; there is also an iodine cough with pains in the chest, which may lead to pneumonia and pleurisy.

We are unable to deny the possibility of the occurrence of these affections of the mucous membranes. It is possible that the potassium iodide excreted with the mucus of the nose, the saliva, and the sweat, is decomposed by means of the nitrate, the carbonates and the salts of the fatty acids of these excretions, and that the iodine thus set free produces a locally irritant effect; but the effect of potassium iodide upon different individuals varies, and after due consideration of the opinions of others, as well of our own experience, it appears to us that many of the ill effects above mentioned are due to the use of preparations, externally or internally, in which free iodine or iodic acid is present; this free iodine or iodic acid produces its ill effects when it is taken, by undergoing vaporization and thus being brought into contact with the mucous membranes above-mentioned, and not after absorption into and excretion from the blood. We can not otherwise explain why it is, that cases treated by us with pure potassium iodide have never shown any of the symptoms above mentioned. In a girl that had been treated for four weeks with potassium iodide, and who had hitherto shown no trace of the iodine catarrh or angina, we began, for the sake of experiment, in the fifth week to use tincture of iodine externally upon the neck, and internally small quantities of a potassium iodide solution. When on the eighth day of the new medication, the above iodine symptoms had set in, the pure potassium iodide treatment was again begun, and soon all of the catarrhal symptoms above mentioned had disappeared.

We might suppose, however, that the condition of the mucous membranes in different individuals varies, and that in *some* people the iodine salt excreted with the mucus finds

conditions favorable to its decomposition, which in others it does not.

Glands.—The power of potassium iodide, when administered for some time, to reduce the size of thyroid glands and also of lymphatic glands which have undergone a simple hypertrophy, has been so frequently observed, that there can be no doubt of it, although we can not explain it. But the idea that potassium iodide has a similar effect upon the spleen, mammary glands, testicles, prostate, ovaries and uterus, seems only to have been deduced from analogy and not based on accurate observation. We could not find even a single case, after a careful search in the literature of the subject, which could be taken to support such a view.

In our own cases we have never seen such a diminution in the size of the mammary glands or testicles, and as to the spleen, prostate, ovaries and uterus, we think it very difficult or almost impossible to make accurate measurements of these. The early menstruation which occurred in the girl reported by Rose, can not, in consideration of the complications in the case, be considered as a proof that iodine has any specific effect upon the female genital organs.

Nervous System and Voluntary Muscles.—Our knowledge concerning the influence of potassium iodide upon these organs is very slight. We ourselves have never seen potassium iodide produce any disturbances upon the human nervous system or muscles ; and since other observers also deny the occurrence of any such disturbances,* (Rose, even after his enormous iodine injections, Boehm and Berg, who found no such disturbances in animals, even after the direct injection into the blood of large quantities of sodium iodide) we think it right at least to doubt the assertions of those who have seen such effects.

The following are said to be the effects upon the nervous system : Benedict reported that he produced in frogs, even by small doses of potassium iodide, paralysis of sensibility and motion which was due to a direct affection of the spinal cord. Somewhat larger doses produce paralysis of the striped muscles of the body and of the muscles of the heart. The nervous paralysis extends gradually from the center to the periphery. The results of these experiments, however, can not yet be made use of to determine this question in the absence of counter experiments made with potassium chloride, to determine whether

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* See page 280,

the above effects are due to the potassium or to the iodine. Sokolowski saw the cerebral vessels in trephined animals dilate and become filled with blood under the influence of potassium iodide, and supposes that the nervous restlessness, headache and sleeplessness, which, according to him, occur in persons poisoned by iodine are due to this cause.

Rilliet asserts that in persons who are susceptible to the influence of the drug, he has found a sort of iodine intoxication, shown by ringing in the ears, neuralgia, beating in the head and even convulsions. Finally Wallace and Rodet assert that one of the effects of chronic iodine poisoning is a sort of general paralysis of the intelligence and motor power.

The whole of the results obtained by Rilliet appear to us to have been chiefly compiled at his study table. His different forms of iodism are partly or entirely repudiated by other good observers (Ricord, Piorry, Gibert), and a number of his assertions are positively false; for example he reports cases of iodine poisoning resulting from the use of cod liver oil, or in consequence of living at the sea shore.

Respiratory Organs.—After the long continued use of iodine in human subjects, according to Wallace, and the intra-venous injection of sodium iodide in dogs, according to Böhm and Berg, there occur pleuritic exudations and œdema of the lungs. Küss believes that the hæmoptysis that sometimes occurs in the course of the iodine treatment is due to the iodine.

Organs of Circulation.—The findings in the single case observed by Rose, which can not be made use of for reasons above stated, can not be explained, as Husemann supposed, by considering the effects as due to the potassium, first because 4.0 grms. of potassium salt could not produce the effects seen in the girl observed by Rose, and secondly because arterial spasm and increased action of the heart are not the results of the action of potassium. According to more recent observations upon animals, the iodine component of the alkaline iodide has no effect upon the heart's action, this being only affected by the alkali component; so that potassium iodide has an effect upon the heart similar to that of potassium* (Bogolepoff). Sodium iodide leaves the circulatory organs entirely intact (Böhm). We ourselves (Rossbach) have observed in men after the long-continued use of sodium iodide, severe palpitation of the heart which lasts some time.

Temperature.—In cases in which the temperature of the

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* Compare page 25.

body was taken after the continued use of potassium iodide, it was found normal. In the cases of the so-called "iodine fever" which have been reported, strange to say, a thermometer never seems to have been used; we therefore consider these reports highly questionable.

Influence upon Nutrition and the Interchange of Materials in the Body.—For a long time the belief that the use of iodine and potassium iodide caused a wasting of the body and disappearance of the fat was so firm, that all the theories of the iodine action were based upon it. Gradually, however, it came to be more and more believed (Ricord, Boinet, and Wunderlich) that not only was there no wasting of the body, but even an increase in the amount of fat of the body resulted from the use of KI. Our experience supports that of Buchheim, who saw no failure in nutrition follow the use of potassium iodide, and as for the assertions of some writers according to whom it does produce wasting of the body, he thinks that in these cases no potassium iodide but a free iodine preparation was given, in consequence of which there were gastric catarrh, loss of appetite and diminished nutrition. Even free iodine has not a direct wasting effect upon the body, but only secondarily in consequence of the gastric catarrh which it produces.

In fact, Rabuteau and Milanesi observed in men to whom they had given potassium or even sodium iodide, that there was a diminution in the amount of urea excreted, in the former case (K I), of 40%, in the latter (NaI) 4–9%; and furthermore, the weight of the body was either increased, or unchanged. v. Boeck, whose methods of observation were faultless, gave a syphilitic young man 1.5 grms. of hydriodic acid, (with 1.49 grms. of pure iodine) for 5 days, without noticing any change in the excretion of urea; but the patient lost 1.4 kilo. in bodily weight. But v. Boeck does not give up the idea that iodine produces an increased metamorphosis of the albuminoids, in spite of the above observation; he believes that, although the iodine does not attack the albumen circulating in the blood, it does that of the organic tissues. In this way the diminution which iodine produces in the size of swollen glands might be explained.

Dosage of Potassium Iodide.—Cases have been reported, in which even small doses of potassium iodide were followed by the appearance of toxic symptoms; while, on the other hand, cases are reported in which 15–25 grms. were taken daily without harm. According to our observations, 5.0 grms. can be taken daily by adults for a long time without any harm resulting.

The usual prescription of 0.1 to 0.5 grm. pro dosi is entirely too small for most diseases.

3.0–7.5 grms. doses, internally, are fatal to rabbits. In dogs, 7.0 grms. produce vomiting, but no other ill effects. An average dose of 0.5 directly injected into the blood, will produce, in dogs, death from paralysis of the heart (Sokolowski).

THERAPEUTIC APPLICATION.

No other of the really active remedies in the materia medica, is so much misused in practice as potassium iodide. Since its recommendation for goitre, amongst other conditions, by Coindet in France, and Formey in Germany, its utility in various diseases has led to its application in a large variety of pathological processes and the fulfilling of various indications. This may be explained, perhaps, by the fact that its physiological action is still far from clear, so that its utility or non-utility in any given affection is based entirely upon experience. Indeed the indications for the use of the drug may be almost formularized in the following manner. If you do not know what drug to give, order potassium iodide.

We do not hesitate, therefore, to say that in one condition only, do we consider the therapeutic value of the potassium iodide to be undoubted, and that is in "tertiary" syphilis, and all organic diseases depending upon it. To these we may, perhaps, add simple (and scrofulous) hyperplastic conditions of the lymphatic and thyroid glands.

In all other conditions, however numerous, we must declare the utility of the iodide of potassium as uncertain and exceedingly doubtful. We have prescribed potassium iodide very frequently, but have never been able to convince ourselves, that in any but the above named conditions the improvement or cure which may have resulted was due to the action of the potassium iodide.

Wallace was the first to recommend potassium iodide in syphilis, and it rapidly gained a well earned reputation in this malady. Although at first used in the various forms of syphilis and often as a substitute for mercury, the drug has shown itself curative only in certain well known forms of the disease, while it cannot replace mercury in other forms of the malady. The whole series of tertiary symptoms are thus amenable to potassium iodide. First of all the bone affections, the "*tophi*" and the "dolores osteocopi"; the more recent these symptoms are, the more rapidly they disappear; old syphilitic

tophi, which have already undergone cheesy degeneration, yield to K I only with the greatest difficulty. So also the gummata in various other organs, such as the brain and liver, the sarcocele syphilitica, the iritis, the affections of the larynx, and finally the syphilitic neuralgias which occur in the tertiary stage, are amenable to potassium iodide. We cannot deny, however, that even here potassium iodide is sometimes ineffective, although the conditions under which it is so are unknown. Ordinarily, however, a cure takes place in those cases in which mercury has been entirely ineffective.

Iodine is of less value in those manifestations of syphilis which appear at a stage intermediate between the second and third ; such are rupia and ulcerating condylomata. In the primary and secondary stages of syphilis iodide of potassium is entirely useless. Experience has shown, however, that when the secondary manifestations reappear, after they have once yielded to thorough mercurialization an iodine treatment is often effective.

It is doubtful, whether the presence of scrofulous symptoms, in addition to those due to the syphilis, is an indication for the use of K I.

If in any individual case of syphilis the potassium iodide is to be effective, we will begin to see the good effects after the use of even small doses (2.5–5.0 pro die). Quantities as large as 15.0 grms. pro die, such as have been recommended, are not at all necessary.

In what manner this drug causes the disappearance of the syphilitic symptoms is unknown. It has been shown that it does not act by increasing the tissue metamorphosis.

Various observers have advanced the hypothesis, that potassium iodide has a favorable effect upon syphilis only because it enables the system to get rid of the mercury which was used in treating the earlier stages of the malady.

This hypothesis is based upon the fact that sometimes, in cases in which mercury had been administered a long time previous, the use of the iodide was followed by salivation, and also upon the theory that the tertiary manifestations of syphilis are to a great extent the result of the antecedent mercurial treatment. Against this hypothesis we have the facts, first, that potassium iodide does cure cases of tertiary syphilis in which mercury has never been used, and secondly, that salivation is not only a sign of mercurialization, but may also be a symptom of *iodism*. We must, therefore, acknowledge the power of the

iodides to cure the tertiary stages of syphilis, although we are unable to explain this action.

Struma was the first pathological condition in which iodine was generally used.

It is entirely without effect in the struma aneurismatica, also when large cystoid cavities have been formed in the glands. On the other hand, it is positive that in the most frequent form, namely simple hypertrophy of the glandular substance (struma lymphatica), even when there is some colloid degeneration no remedy is more effective than potassium iodide. It should be given internally, if no counter-indications exist (such as digestive disturbances, tendency to tuberculosis, etc.,) and should also be painted on externally in the form of the tincture of iodine (compare with what is said under this preparation).

Much is said concerning the use of iodide of potassium, iodide of iron, etc., in scrofula ; some praise its efficacy in this malady, while others, very recently, condemn it as useless. Shortly after the introduction of iodine as a remedy, the view began to obtain that it was very effective in the various forms of scrofula, and that it was best borne by individuals of a lax constitution, in whom there is no sign of an irritable disposition or any tendency to congestions or venous plethora (G. A. Richter). It is most useful in what was formerly termed the "torpid" form of scrofula, the physiognomy of which is the well known puffed face, thick lips, etc. Even in these cases it has a varying influence over the different scrofulous manifestations. Potassium iodide is most effective in the scrofulous tumors of the glands, especially when they are not ulcerated. It is given internally, while the tincture of iodine is used externally.

Our experience has not yet been sufficiently large to enable us to express a positive opinion concerning the value of injections of ticture of iodine into glandular tumors. It (KI) is less reliable in other forms of inflammation of the skin (impetigo, lupus), diseases of the mucous membranes, and affections of the bones ; but even in these cases we have seen favorable results. The best dietetic and hygienic regulations should be observed, for to these we believe much of the good effect can be ascribed. We should here add that many old ulcers, which have withstood the most varied treatment, and the subjects of which give no syphilitic history or symptoms, are improved and healed under the influence of iodides.

Potassium iodide internally and iodine externally have been

used in hypertrophy of other glandular organs, and with some success. Especially so in simple hypertrophy of the mammæ and testes. Such observations have given rise to the belief which was formerly held that even malignant growths (carcinoma, sarcoma) are made to disappear by means of iodine. But we regret to say that this idea has not been confirmed. The iodine compounds have also been used in the treatment of hypertrophy of various organs depending upon chronic inflammatory processes, and, it is said, with some success—so in metritis, prostatitis, etc. When a good result may be expected and when not we are unable to define. We should here mention the use of potassium iodide in general corpulence. Its action here, however, is not to be depended upon, and besides this we have better remedies for this purpose.

In phthisis, iodine and iodide of potassium were formerly and again recently given, both internally and in the form of inhalation, and vapors. Of the results of this treatment we can only say that iodine not only does not heal or arrest tuberculosis, but is often directly injurious ; for iodine causes even in healthy persons hæmoptysis and bronchitis, much more so in tuberculous subjects. It is positive that the use of iodine in these patients generally allows the disease of the lungs to advance more rapidly, or if there be only a tendency to tuberculosis, without the presence of tubercles, the latter are developed under its use. This drug should therefore be avoided in these patients.

Potassium iodide internally and iodine externally are very much used in the various forms of rheumatism, but it is exceedingly doubtful whether any benefit results from their use. In acute articular rheumatism it is entirely without effect, while in acute muscular rheumatism it seems to be without any noteworthy benefit. On the other hand, it seems to be of some value in chronic forms of rheumatism, and the vague pains of non-febrile muscular rheumatism often disappear quite rapidly under its use. But even this effect is not always attained by the use of the drug, and we have more often seen it fail than succeed. Some observers have had good results with potassium iodide in chronic affections of the periosteum and the fibrous structures of the joints. But here, again, the drug is sometimes entirely ineffective, in spite of its energetic application, and we are unable to foretell the conditions under which it may be expected to succeed. If the so-called rheumatic deposits are already present, or if the case be one of *arthritis nodosa* deformans, the iodine is entirely without effect.

Present experience does not support the idea that this drug possesses any advantages over other preparations in the treatment of gout. In recent times it has been recommended in typhus, as well as malarial intoxication (Willebrandt.) The observations concerning this point, however, have been too few, and the few reports that have been made do not speak in favor of this application.

Potassium iodide and iodine are much used in exudative inflammations of serous membranes, with the idea that these remedies promote absorption ; they are thus used in pleurisy, peritonitis, pericarditis and meningitis. KI is given in these cases after the febrile symptoms have disappeared, the appetite has been restored, and only a fluid exudation remains. An impartial judgment, based upon observation, would teach that potassium iodide exerts very little of the above mentioned effect, and is therefore, for this purpose, almost useless. No observation has positively shown that it causes reabsorption of the exudation in meningitis, while in pleurisy we have better means for this purpose than potassium iodide ; its utility in pericarditis and peritonitis is equally uncertain. In all of these conditions, and especially in pleuritic exudations and in peritonitis iodine is used externally in the form of tincture—that by its means the pains are somewhat alleviated, while it also acts as a counter-irritant to the existing inflammatory process, is not to be denied ; but that it ever hastens the absorption of the exudation is just as doubtful as is the production of a similar effect by the internal administration of the KI.

Equally unproved is the utility of potassium iodide in conditions of hyperplasia of the connective tissue of various organs, and the diseases depending upon this condition. We have never seen any reason to suppose that the administration of potassium iodide has ever interrupted the course of a chronic nephritis, cirrhosis of the liver or a chronic myelitis. It is prescribed in these conditions in the absence of better remedies.

Potassium iodide is also used internally in neuralgias, especially of the fifth nerve, and above all in sciatica. We cannot deny that a good result is obtained by its use in some cases. In may be expected in cases in which the neuralgia depends upon the pressure of a syphilitic exostosis upon some nerve trunk, or upon a syphilitic neuritis, and sometimes also in cases of so-called rheumatic or idiopathic neuralgia, especially those that have lasted a very long time. But we must confess that although we have used potassium iodide in neural-

gias very often. We have seen but few cases in which we were positive that improvement resulted from its use.

Leyden has used potassium iodide with good effect in those cases of asthma bronchiale in which he found the crystals which he was the first to describe. Our own experience leads us to confirm this result. It is perhaps owing to these cases that potassium iodide has been recommended in emphysema pulmonum.

Furthermore, iodide of potassium has been used in the treatment of chronic metallic poisoning. In most of these cases its utility has not been proved. Only in mercurial and lead poisoning have good results now and then been noted. Annuschat found in a woman and also in a dog suffering from lead poisoning increased excretion of lead in the urine, on the administration of potassium iodide.

Dosage and Preparations.—1. Potassium iodatum, internally, from 0.5—1.5 pro dosi in pill or solution 2–3 times a day. Baths, with potassium iodide added, are entirely useless.

2. Unguent. potassii iodati—20 parts of KI., 1 part of sodium sulphurosum dissolved in 15 parts of aqua dest. and rubbed up with 165 parts of fat. Quickly turns rancid, and is readily decomposed. It should therefore always be freshly prepared. This ointment is inactive. If a local iodine application is needed, we should always prefer the tincture.

3. Iodine Waters.—For a long time much has been said concerning the iodine contained in some sodium chloride springs. Indeed, some have ascribed the good effects of sea air to the iodine which it contains (evaporated from the sea water.) The waters most praised for their iodine component are Kreuznach, Krankenheil, Durkheim, etc.

A little consideration will show how little likely it is that the very small quantities of iodine, that can be thus introduced into the body with the sodium chloride spring waters, have any effect. It is positive that a favorable effect has not been proved to depend upon the iodine, and that whatever effect is obtained results just as well from the use of pure sodium chloride waters.

3. SODIUM IODIDE—SODIUM IODATUM.

That potassium iodide is the preparation chiefly used in medicine is only an accident. Indeed if the iodine preparation is to be given for a long time in large doses the sodium salt should be preferred to that of potassium for reasons given above. In fact we have used sodium iodide almost exclusively for years with the usual therapeutic results.

APPENDIX TO THE IODINE COMPOUNDS.

Iodic acid—HIO_3 and sodium iodate, $NaIO_3$.—Binz has recently contributed his observations concerning these bodies. According to him

iodic acid is an antiseptic, at first because of the active oxygen which it contains, and later on because of the free iodine which remains. Sodium iodate, therefore, given internally in putrid fevers acts promptly, although only temporarily, as an antipyretic.

Sodium iodate, like iodoform, also has a confusing effect upon the brains of animals, and a paralyzing effect upon the respiratory center. (The results of the latter can be warded off by artificial respiration.) Binz explains these effects as depending upon the action of free iodine upon the nerve centers. Small doses have no effect upon the heart—large ones, however, produce death by paralysis of the heart.

The iodates are therefore more poisonous than the iodides (sodium and potassium iodide), because all of the albuminoids reduce the former, thus giving rise to the formation of NaI in company with the $NaIO_3$, which, coming in contact with a free acid, as for example carbonic acid, forms iodine carbonate. While only some tissues, such as for example pathological ones, set free iodine from the iodides. Melsens and Rabuteau report cases of serious poisoning, with vomiting and purging, produced with preparations of sodium and potassium iodides, which were rendered impure by admixture with iodates.

According to Binz it would be well to try the effect of the sodium iodate, on account of its strong action, in all cases in which the officinal iodine preparations have hitherto been used.

Concerning the ethyl, methyl and amyl iodides as well as iodoforms, we refer to the alcohols and their derivatives.

Treatment of Iodine Poisoning.—We have no extended experience concerning the treatment of iodine poisoning. We would use starch and perhaps albumen as antidotes. Further treatment would have to be governed by circumstances, such as the counteraction of the gastro-enteritic symptoms, etc. There is no regular plan of treatment of chronic iodism. As a rule the symptoms disappear gradually as soon the administration of the drug has ceased.

THE CHLORINE COMBINATIONS.

I. CHLORINE—CHLORINE WATER.

Chlorine, Cl, occurs widely distributed in the inorganic and organic world, especially in combination with sodium. It is a yellowish green, condensible gas, which is absorbed to a greater extent by water the lower the temperature, thus forming a yellowish-green solution, called chlorine water. Chlorine water has the odor of the gas, can only be kept unchanged in the dark, and decomposes rapidly in the light, hydrochloric acid being formed and oxygen set free. 100 parts of the officinal chlorine water are said to contain 0.4 parts of chlorine.

Physiological Action.—The chief effects of chlorine can be explained by its close relationship to hydrogen. It withdraws hydrogen from the organic molecules with which it is brought in contact, and forms hydrochloric acid while in place of the hydrogen chlorine enters, all of which leads to the destruction of the original molecular structure.

In this manner it produces a caustic effect upon the animal tissues, a coagulating effect upon the albuminates, the blood and the adhesive substances—a destructive and bleaching action upon all vegetable and animal colors, even that of the hair, while it destroys all chemical and organic bodies, which cause and maintain decomposition, as well as the gases of

decomposition and the lowest organisms, thus suspending decomposition and destroying the odors of decomposition.

In this way may be explained all of the symptoms of chlorine poisoning, either as the result of changes in the tissues or of reflex reaction.

When the skin is brought in contact with chlorine it becomes inflamed. Then ensue prickling, burning, formation of blisters, erysipelatous infiltration, and superficial destruction with the formation of a soft eschar of entirely destroyed tissue. Chlorine can also be absorbed by the unbroken skin.

Upon the mucous membrane of the respiratory passages its direct action is to produce a sensation of a very sharp odor, burning and pain in the chest, As reflex results of its inhalation we have lachrymation, sneezing, cough, spasm of the vocal cords (which is soon over, however, contrary to what was formerly believed so that respiration can again be carried on (Falk)), and difficulty in breathing.

Long continued inhalation of the gas is followed by chronic bronchitis, acute inflammation of the lungs and hæmoptysis.

Digestive Organs.—Internally administered, chlorine gives rise to the formation of hydrochloric acid (see this) which furthers digestion and produces slight constipation; the fæces are sometimes said to be decolorized. In larger doses, it has an inflammatory effect upon the mucous membranes of the digestive canal, producing a caustic action, with the results enumerated under the head of the caustic alkalies.

General Effect.—It is not probable that chlorine, when inhaled, remains as such in the blood for any length of time. Cameron, however, asserts that after chlorine poisoning the cranial cavity still smells of chlorine, while Wallace says that after chlorine poisoning, the urine which is passed has the power of decolorizing plants.

The importance of chlorine to the life of the animal organism, has already been discussed under the head of sodium chloride, since this is the form under which it chiefly exists in the animal body.

Therapeutic Application.—The formerly extended use of aqua chlori internally is now very much diminished. This preparation is entirely superfluous as an internal remedy. There is no condition in which it cannot be replaced by better and more successful remedies. It is no longer given in typhoid conditions and septic fevers with decomposition of the blood, nor in scarlet fever, in jaundice and many other diseases in which it was formerly given. It has not been shown that it exerts any favorable influence upon the diseased process in dysentery with foul smelling stools, although it may be prescribed in this condition in consideration of the good results obtained by some observers. Some of the older practitioners give chlorine water in some forms of dyspepsia and gastric catarrh, but we have been unable to convince ourselves that there is any good to be derived from its use. Chlorine gas (inhaled) has also been used as an antidote to poisoning with hydrocyanic acid and sulphuretted hydrogen. The results of experiments concerning this subject are diametrically opposed to each other, while we have no clinical experience upon which an opinion might be based. Chlorine inhalations were very much used in the 30th to the 40th year of this century in the treatment of chronic diseases of the lungs. The observations of Louis and Stokes have long ago shown their non-utility and even their non-applicability; even in chronic bronchitis they can be replaced by better remedies which do not themselves cause irritation and coughing.

Externally *chlorine* water is very much used, in conditions in which also *chloride of lime* is used, and which will be discussed under the head of that

drug. In some conditions it should be preferred to lime chloride, especially in certain conjunctival affections (v. Graefe). It is also used in contagious ophthalmia, in old trachoma and in torpid infiltrations which have a tendency to ulceration. In conditions of irritation it is contraindicated. Chlorine water is also a good disinfectant in poisoned wounds (dissecting wounds, bites of poisonous animals, etc.,) but is not as energetic, in these cases, as other materials.

To obtain the deodorizing, etc., effect of chlorine gas we should make use of the chloride of lime (to which we refer).

Dosage.—Aqua chlori, internally 2 0–5.0 pro dosi, mixed with water; externally, pure or mixed with various amounts of water. As an eye wash (of the officinal strength) dropped into the eye once or at most twice a day. In ophthalmia neonatorum, 1 teaspoonful to 5 tablespoonfuls of water or chamomile tea (for washing the eye).

2. CALCARIA CHLORATA—HYPOCHLOROSA—CHLORIDE OF LIME.

The preparation prescribed by the German pharmacopœia is a mixture of many chemical bodies. It is made by passing chlorine gas over hydrated lime. The chlorine combines with the oxygen of a part of the lime to form hypochlorous acid, which combines with a portion of lime. The deoxidized lime (calcium) combines at the same time with an atom of chlorine—$2CaOHOH+4HCl=CaCl_2+(ClO)_2Ca+2H_2O$—that is a mixture of lime hypochlorite and calcium chloride, with which there is still mixed some hydrated lime. The statement that there is 25% of chlorine in this preparation is exaggerated (Mohr).

It is a white powder, having a mild chlorine odor, and which is only partly soluble in water. Upon the addition of hydrochloric acid large amounts of chlorine gas are given off.

Physiological Action.—The action of lime chloride is a compound of that of chlorine water and lime water, of which it is really a mixture.*

Therapeutic Applcations.—For internal use the preparation is entirely superfluous, for there is no condition in which it has been found beneficial. But its external application is very extensive. It may be used with good effect as a dressing for indolent ulcers, especially in those of the leg where there is little secretion, and the granulations are pale and show little tendency toward a healing process. It is also used as a dressing for putrid bed sores; also in noma, gangrene and diphtheria, after the more energetic remedies have already been used, and have left a simple, ill-appearing, ulcerating surface. Although formerly used in gonorrhœa, lime chloride has been recently warmly recommended as an injection in old cases of gleet after all inflammatory symptoms (especially pain) have subsided; the amount of the secretion which may be present is a matter of no importance. Our experience in the use of the remedy in these cases is favorable. Injections of lime chloride solutions are also of value in foul smelling vaginal discharges. As to the importance of lime chlcride, from its free chlorine, as an antidote to hydrocyanic acid poisoning, we refer to what was said under chlorine.

Chloride of lime is one of the most useful disinfectants. It is a very good deodorizer, and is used for this purpose in dead houses, sick rooms and and every place where there are foul odors. Also used for washing purposes after dissection and after handling foul wounds. We should be careful, however, about using it in rooms in which patients lie sick with disease of the respiratory organs.

* See pages 299 & 85.

The use of chloride of lime as a disinfectant (cholera excrements, typhus, etc.,) has been very much diminished in recent times by the fact that we now have much more active substances (such as mineral acids, carbolic acid, etc.)

Dosage and Preparations.—Calcaria chlorata, internally, from 0.05 to 0.5 pro dosi in pastilles. In solution its use is impracticable (on account of its only partial solubility). Externally it is used as an injection in gonorrhœa in $^1/_{10}$–$^1/_5$ % solution. As a dressing for ulcers, etc., in 2–5 % solution. For disinfecting sick rooms lime chloride should be placed in cups and moistened with water or hydrochloric acid.

2. Fumigatio chlori, chlorine fumigation (officinal). For strong fumigation, take equal parts by weight of brownstone and sodium chloride and moisten with double the quantity of sulphuric acid diluted with 1 part of water. For weaker fumigation add some vinegar to chloride of lime which has been mixed with water.

3. Liquor sodii hypochlorosi s. chlorati—Sodium hypochlorite—Bleaching fluid.—Potassium and sodium hypochlorites, both of which have hitherto been known only in solution (Eau de Javelle and Eau de Labarracque) are used by us only in the arts for bleaching purposes, while in England and America they are used for the same purposes as lime chloride. Recently it has been recommended as an excellent remedy for chronic gonorrhœa (Fraenkel) in 2–5 % solution. Whether the preparation is to be preferred to lime chloride, is left for experience to determine.

SULPHUR AND ITS COMBINATIONS WITH ALKALIES AND HYDROGEN.

Pure sulphur, as long as it remains unchanged in the organism, gives rise to almost no general or local effects. Most of the physiological effects observed from the use of sulphur and its combinations with the alkalies, are due to the sulphuretted hydrogen formed from them in the body. We shall therefore begin with the consideration of the physiologically active sulphuretted hydrogen, because we shall thus be enabled the better to understand the action of the sulphur and alkaline sulphides.

I. SULPHURETTED HYDROGEN—HYDROGENIUM SULPHURATUM.

Sulphuretted hydrogen, H_2S, is a colorless gas, which reddens blue litmus paper, for which reason it is counted among the acids and called hydrothionic acid. Water absorbs 2 to 3 parts by volume of the gas (sulphuretted hydrogen water, aqua hydrosulphurata).

Physiological Action.—This gas, which has so disgusting an odor and taste, is an almost constant, although the least, constituent of the human intestinal gases which are developed during digestion, especially of meat, in the lower portions of the intestinal tract. It gives the characteristic odor to rotten eggs, and is formed in large quantities in privies and cesspools. It is absorbed with equal readiness by the skin and the mucous membrane of the respiratory and digestive canal.

Its poisonous effect is not slight, but is overestimated when it is compared to that of hydrocyanic acid. Chemists and excavators often remain for some time in an atmosphere quite heavily charged with H_2S apparently without being injured. The fatal limits for human beings are unknown, bnt dogs are said to die in an atmosphere containing more than 1-10 % of H_2S.

The causes of the powerful poisonous effect which it exerts are to be found partly in the change which it produces in the composition of the blood, and partly in a direct action upon the nervous centers.

Blood and Nervous Centers.—When oxygenated blood is mixed with sulphuretted hydrogen, the oxyhæmoglobin is immediately deprived of its oxygen, and in the spectrum the absorption band of reduced hæmoglobin appears; the latter is then converted into a material resembling hæmatin, but redder in color, and which does not absorb oxygen from the air; finally a body is formed which contains much sulphur, is of an olive-green color in thin layers and brownish-red in thick layers; at the same time sulphur and an albuminoid material are deposited. It is a remarkable fact that hæmoglobin solutions which are free from oxygen are not decomposed, even when sulphuretted hydrogen is bubbled through them for some time. (Hoppe-Seyler).

The alkaline phosphates and carbonates (not the alkaline chlorides) which are present in the blood serum, are changed under the influence of sulphuretted hydrogen into sulphur compounds, and if oxygen be present, into hyposulphites and sulphates. (Diakonow and Hoppe-Seyler).

These serious disturbances in the blood can be produced in cold-blooded animals even during life by the action of sulphuretted hydrogen. If frogs be placed in an atmosphere of sulphuretted hydrogen, the blood is seen to turn black, and finally the blood corpuscles being destroyed, to a green color. Warm-blooded animals, however, die from paralysis of the nerve centers and heart long before the blood has undergone any such alterations. For this reason the blood is found venous in color even in the arteries immediately after death, yet the oxyhæmoglobin bands have not entirely disappeared.

Death from sulphuretted hydrogen in warm-blooded animals is therefore only partly due to suffocation. It probably depends in part upon a specifically injurious effect of the sulphuretted hydrogen upon the various nerve centers, especially those of respiration and circulation. For the blood is never entirely free from oxygen even after death, as is the case with those who have suffered suffocation. Paralysis of the brain, heart and respiration set in more rapidly in sulphuretted hydrogen poisoning than in suffocation; again, death occurs even if plenty of oxygen be supplied to the animal, while salt frogs that have been deprived of blood die with the same symptoms as normal frogs. (Lewisson.) Finally it was shown by Schoenbein that sulphuretted hydrogen, like hydrocyanic acid, deprives many organized bodies (such as seeds, fresh roots of plants, the ferments, such as the yeast plant and also the blood corpuscles) of their power of decomposing the hydrogen dioxide, H_2O_2, into water, H_2O, and ordinary oxygen (catalytic action); and since these substances lose their essential properties with the loss of catalytic power, we may conclude that sulphuretted hydrogen exerts a poisonous effect upon many other portions of the body, besides the blood.

Toxic Symptoms.—Small but not fatal quantities inhaled or absorbed from the intestinal canal, as happens in autogenetic poisoning from sulphuretted hydrogen, absorbed into the blood from the intestinal canal where it has been formed in excessive quantities from the fæces (Senator), cause headache, dizziness, paleness of the face, frequent and weak pulse, eructation of gas, a tendency to vomit, pains in the abdomen and diarrhœa.

The intestinal nerves especially appear to be very much irritated even by *small quantities* which produce no other disturbances. We know people *who whenever* they inhale this gas suffer from by diarrhœa. We may

therefore consider that the sulphuretted hydrogen, normally contained in the intestinal gases, is important for producing intestinal peristalsis.

The statements that small doses give rise to increase in temperature, a feeling of pressure over the chest, increased secretion of the sweat and salivary glands, and increased excretion of nitrogen, that is to say of urea, and that they have a favorable effect upon parasitic and septic diseases, need further confirmation.

Fatal doses produce the following effects in cold-blooded animals: A quickening followed by a slowing of the respiration; slowing and weakness of the heart's action; finally there is a general relaxation of the body although for a long time the nerves and muscles still retain their irritability. The hearts and muscles which have been cut out of frogs become rapidly paralyzed in sulphuretted hydrogen; the muscles indeed become stiff and greenish in color.

In men and other warm-blooded animals such doses cause loss of consciousness, appearance of suffocation, severe dyspnœa followed by general convulsions with dilatation of the pupils and death. Death is due to asphyxia, that is to say to paralysis of respiration. The application of artificial respiration may therefore save the lives of these cases. (Falck, Kaufman and Rosenthal).

Excretion from the body.—Smaller poisonous doses of sulphuretted hydrogen are, owing to their conversion in the blood into sulphates (Diakonow) excreted as such with the urine. When larger quantities are introduced into the body, Senator thinks that they pass out under their own form with the sweat, expired air and urine.

Therapeutic Application—Internally, in the form of aqua hydrothionica or hydrosulphurata, sulphuretted hydrogen is entirely superfluous and very little used.

On the other hand the value of sulphur waters is estimated according to the percentage of this gas which they contain.

Sulphur waters generally contain only traces of free sulphuretted hydrogen; in some springs there is a larger percentage, but the quantity is still very small. In these waters there are found also sulphur alkalies, such as sodium, calcium and magnesium sulphide, from which sulphuretted hydrogen can be developed in the intestine, but these sulphur alkalies are also present, only in small quantities. The percentage of other salts contained in these springs is so small that they do not impart to the waters any peculiar effect. In a few only is sodium chloride present in active quantities (those of Aachen, Burtscheid, Baden in Switzerland, and Mehadia). The free carbonic acid is so small in quantity that it has no influence upon the effect of the water. The temperature which in some of the waters is quite high, is an important element, so that the sulphur waters are divided into hot and cold.

The sulphur waters are used for bath and drink "cures."

For bathing purposes it is only the percentage of free sulphuretted hydrogen which is of importance, but this is so small, even in the most celebrated sulphur waters, that the therapeutic effect really observed probably depends upon other elements (Braun). These active elements are probably, 1st, the bath as such; 2d. the high temperature (Aachen, Burtscheid, Baden in Switzerland, Baden in Vienna, Aix and Luchon); 3d. in some springs the percentage of cooking salt (Aachen, Burtscheid, Baden in Switzerland and Mehadia); and in some the high altitude of the spring (Baths of the Pyrenees). Similar elements have an important influence in the effect of sulphuretted hydrogen drink cures, although in these perhaps the slight amount of sulphuretted

hydrogen formed in the intestine from the sulphur alkalies and sulphates adds its quota to the general effect of the waters.

The most important of the sulphur waters are—Aachen, 55°C., contains a very small amount of sulphuretted hydrogen and also an equally small quantity of sodium sulphide, some sodium and potassium sulphate and a considerable quantity of sodium chloride. 2. Burtscheid, 58°, in the neighborhood of Aachen, is analogous to the latter in composition, except that it contains a little more sodium sulphide. 3. Eilsen in Bueckeburg. 4. Nenndorf, in the Province of Hessen. 5. Weilbach, in Wiesbaden. 6. Langenbruecken, in Baden, cold springs. 7. Baden, near Vienna, 35°C. 8. Baden, in Switzerland, 46°C. In the Pyrenees we have Eaux-Bonnes, Eaux-Chaudes, Saint-Sauveur, Bareges, Bagneres de Luchon. In Savoy, Aix-les-Bains. In Hungary, Mehadia, Pystian, Gross-Wardein and Toplitz. Both of the latter with a large percentage of sulphuretted hydrogen.

Sulphur baths are of course used and recommended in a large number of pathological conditions; whether, however, a peculiar, specific effect can be ascribed to them, that is to say, whether they exert from the sulphur which they contain, a different effect from that of other baths, such as the indifferent and the sodium chloride thermal baths, is a point which has not yet been proved. The indications for their use are similar to those for the use of the indifferent and sodium chloride thermal baths, and in some pathological conditions they are just as useful as the latter, but impartial judgment does not show that they are any more useful. The conditions in which they are of use are:

1. The various chronic rheumatic affections. 2. Gout. 3. Various diseases of the nervous system, as already indicated under the head of sodium chloride waters. 4. In a series of chronic diseases of the skin (acne, psoriasis, eczema, prurigo, pustulous eruptions, etc.) sulphur baths do no more good, indeed, sometimes less good, than indifferent baths. 5. In syphilis they are said to benefit in a variety of ways; not only are they expected to cure old and inveterate sores of syphilis, but are said at the same time to bring to the surface latent syphilitic symptoms, and also to be of use in chronic mercurial poisoning. As is well known, Aachen has a great reputation in these cases.

6. The sulphur baths are also very much used in chronic metallic poisoning; that is to say, in mercurial poisoning. According to the observations of Tanquerel a therapeutic advantage is to be expected, above all, in lead arthralgia. He reports out of 35 cases of lead arthralgia treated on the expectant plan of treatment, 22 recovered in from 10–12 days; on the other hand 80 out of 90 patients treated with sulphur baths recovered in from 4–5 days. Sulphur baths are said to be equally effective in lead tremor, anæsthesia and general wasting—they can also be used in lead palsy together with electricity. Upon the other symptoms of lead poisoning such as lead colic, baths seem to have no direct influence. Less accurately defined are the indications for their use in the various forms of mercurial poisoning, but they have been most used in the general mercurial cachexia. Here we must again call attention to the fact, that in chronic metallic poisoning, the utility is not seen in any specific action of the sulphur baths, but simply in the warm baths as such. Guentz recently again recommends sulphur drink cures and sulphur baths as a cure for mercurial poisoning.

Sulphur "drink cures" are used in many conditions, without any special effect being expected from their use. The indications for the use of these "cures" are chronic catarrh of the pharynx and respiratory passages, stasis of the circulation of the portal vein (abdominal plethora) and finally chronic metallic poisoning.

2.—POTASSIUM SULPHIDE—POTASSIUM SULPHURATUM.

The German Pharmacopœia gives two preparations for internal and external use.

1. Potassium sulphuratum s. hepar sulphuris ad usum internum.
2. Potassium sulphuratum s. hepar sulphuris ad balneum.

These two preparations resemble each other, but the former is the purer of the two; they are not simple chemical bodies, but a mixture of the various sulphides of potassium, as for instance the triple sulphide (K_2S_3) and the sulphate and hyposulphite of potassium.

They are of a greenish yellow color, have a disgustingly bitter, half alkaline and half sulphur taste and are easily soluble in water (1 : 3) and in alcohol.

Physiological Action.—Upon the healthy and diseased skin potassium sulphide has an irritating effect.

In the stomach and intestinal canal it is readily decomposed, sulphur and sulphuretted hydrogen, triple sulphide of potassium and many other potassium salts being set free, so that the part which each of these bodies takes in the final effect is difficult to estimate. The whole exert effects similar to those of sulphuretted hydrogen. Locally the potassium components produce a stronger inflammation, indeed almost a caustic effect upon the mucous membranes, a feeling of warmth in the œsophagus and severe gastro-intestinal inflammation with its consequences.

Therapeutic Application.—For internal use the remedy is entirely superfluous; there is no condition upon which it exerts any decided effect, or in which it has any advantage over other less dangerous remedies (on account of the possibility of sulphuretted hydrogen poisoning). Externally potassium sulphide is used in various diseases of the skin. In the itch, in which it was formerly very much used, it is now superfluous. We have to-day remedies which act much more quickly and much more positively. In other chronic diseases of the skin its utility is only slight and second to that of other remedies.

In acne rosacea, however, ointments of the sulphur alkalies are very advantageous.

Baths of potassium sulphide prepared at home are frequently used in chronic rheumatism of the muscles as well as the joints and with good effect. How much of the effect is due to the warm water and how much to the potassium sulphide is uncertain. Nor is it positive that these baths are more effective than other remedies and methods of treatment of chronic rheumatism.

Dosage.—Potassium sulphide, 0.05–0.5 pro dosi (2.0 pro die) in pill and solution. For bath, 50.0–200.0 to a bath. Sometimes a little sulphuric acid is added to the bath—5.0 of acid. sulphur. to 30.0 of pot. sulphide. Sulphuretted hydrogen gas is then developed, for which reason great care should be taken with this method of treatment. As a wash, 5.0–15.0–100.0 grms. For an ointment, 1 part to 5 : 10 parts.

3.—SULPHUR.

Sulphur is a yellow, colorless and very brittle body, which occurs under two modifications—the crystalline and amorphous.

Crystalline sulphur is insoluble in water, only slightly so in alcohol, ether and carburetted hydrogen, most soluble in sulphide of carbon. Amorphous sulphur is entirely insoluble in all of these fluids.

The German pharmacopœia gives very unnecessarily three preparations.

1. Sublimed sulphur, sulphur sublimatum (flowers of sulphur). A mixture

of crystalline and amorphous sulphur, which is often rendered impure by admixture with arsenic and selenium or with sulphurous acid, and can therefore only be used externally.

2. Purified, sublimed sulphur, sulphur depuratum (purified flowers of sulphur) which is free from the impurities of the first preparation.

3. Sulphur precipitated from the sulphide of calcium by hydrochloric acid, sulphur precipitatum, milk of sulphur. In this preparation the sulphur exists in a state of very fine subdivision. For this reason and because it contains sulphuretted hydrogen it has a stronger effect than any of the other two preparations.

Internally we may use the purified or precipitated sulphur.

Physiological Action of Sulphur upon the Organism.—A large portion of the sulphur introduced into the stomach passes off with the fæces unchanged. Small quantities appear to be changed in the intestinal canal into the alkaline sulphides and sulphuretted hydrogen; we reach this conclusion from the fact that after the administration of sulphur the fæcal masses have a strong sulphuretted hydrogen odor, while the flesh of sheep fed upon sulphur has the smell and taste of that gas, and because the skin and expired air of men and animals that have taken sulphur give off the odor of sulphuretted hydrogen.

The alkaline sulphides and sulphuretted hydrogen gas absorbed into the blood appear again in the urine as sulphates. In larger quantity (½ of the amount of sulphur taken) after the precipitated sulphur, and in smaller quantity (½) after the sublimed sulphur. The more rapidly the cathartic effect sets in, the less sulphur there is in the urine and the more in the fæces (Buchheim-Krause).

Effect upon the Skin and Mucous Membranes.—Sulphur can only exert an effect through the skin by being converted to a certain extent into sulphuretted hydrogen, (under the influence of the fat and warmth) which can be absorbed by the skin.

All of the sulphur preparations, on account of their insolubility in water are tasteless and odorless—to this precipitated sulphur is an exception, this having the taste and smell of H_2S.

The only positively determined effects are those which it exerts upon the intestine. It causes abdominal pain, increased intestinal peristalsis and soft fæcal passages. Severe local symptoms of irritation have not been observed to follow even very large doses.

A general effect, if any takes place, would result from the small quantities of sulphuretted hydrogen, and would therefore be similar to that described under that drug.

Therapeutic Application.—Formerly sulphur was a remedy very much used in inflammations, gout, rheumatism and liver troubles. Careful observation has not shown that it possesses any of the qualities which have been ascribed to it; it is therefore now only used as a laxative. It is very improbable that it possesses any advantages over other cathartics, such as the salines, in certain conditions of which chronic constipation, hæmorrhoidal tumors and liver affections are examples. The great power formerly ascribed to sulphur as "anti-hæmorrhoidal" has not been confirmed by impartial observation. As a laxative it should be combined with other substances, such as salines, rhubarb, etc. Formerly sulphur was given in every possible affection of the lungs, but now it is only occasionally administered in the form of Kurella's powder. Recently it has again been recommended in the treatment of diphtheria; flowers of sulphur are to be blown upon the dis-

eased portion of the pharynx. This procedure is thought to be effective because of the formation of sulphurous acid on the contact of the sulphur with the moist mucous membrane. It is used in diphtheria for the same reason as many other remedies, because it has been recommended; its utility is entirely problematical.

Externally sulphur was until recently considered of great importance in the treatment of scabies; it was always an element in every method of treatment proposed. Sulphur depuratum has, however, no effect upon the itch mite, and the good results attained from its use probably resulted from the simultaneous application of other remedies and the mechanical effect of the rubbing. To-day, when we have far superior remedies in the balsams, sulphur is entirely superfluous in the treatment of scabies.

Dosage and Preparations.—1. Sulphur depuratum, flores sulphur. loti, from 0.5–2.0 (10.0 pro die) in powder. As a laxative from 4.0–6.0 pro dosi. 2. S. sublimatum. 3. S. præcipitatum, lac sulphuris, from 0.2–1.0 (5.0 pro die; as a laxative from 2.0–4.0 pro dosi. 4. Unguent. sulph. simplex, 1 part of sulph. dep., and 2 of ad. suill. 5. Unguentum sulphuratum compositum, 1 part of sulphur, 1 part of zincum sulphuricum and 8 parts of adeps suillus. 6. Oleum. lini sulphuratum, 1 part of sulphur sublim., 6 parts of ol. lin.

APPENDIX TO SULPHUR.

The sulphur compounds of sodium and ammonium have also the effect of sulphuretted hydrogen.

Some of the calcium combinations with sulphur also have the power of dissolving tissues of the animal body, such as the hair, feathers and nails; it converts them into a soft, jelly-like mass, which can be easily rubbed off. Husemann recommends the calcium hydrosulphide as the best for this purpose $Ca(SH)_2$.

Treatment of Sulphuretted Hydrogen Poisoning.—Sulphuretted hydrogen poisoning occurs most frequently in workmen working about privies and cesspools. The treatment is that ordinarily adopted in asphyxia. The patient should be rapidly removed from the injurious atmosphere and artificial respiration practiced. If this method of treatment is ineffective, transfusion should be tried. If materials containing sulphuretted hydrogen have been swallowed, or if the poisoning be due to potassium sulphide, the stomach should be first cleared of its contents; in these cases the subcutaneous injection of apomorphine is the best emetic, while the administration of tartar emetic should be avoided, because of its ready decomposibility.

CARBON—CARBO.

1. Carbo pulveratus, wood made by submitting the lighter woods, such as those of the lime tree and the poplar to slow combustion.

2. Carbo animalis, animal carbon, formed by roasting veal and ⅓ as much of small bones together.

Physical and Physiological Action.—Wood carbon, dry and freshly burned charcoal, has the property of absorbing gases and vapors of various sorts to 100 times its volume. One volume of box wood carbon, for instance, is able to absorb 10 volumes of oxygen, 35 volumes of carbonic acid, 55 of sulphuretted hydrogen and 90 of ammonia. When saturated with one gas or with water, its power of absorption for any other gas is suspended. Moist charcoal, or such as has lain for a long time in the air, is therefore useless for

absorbing any other gas. In consequence of these physical properties charcoal is able to bring about chemical combinations in the dark, which generally take place only in the sun-light. In this manner charcoal saturated with chlorine, is able to bring about the formation of hydrochloric acid, when hydrogen is brought in contact with it.

Charcoal has also a great affinity for some materials in solution, such as coloring matters, bitter principles, ætherial oils and septic materials ; so that many variously colored fluids are decolorized by being filtered through it ; such as ink, red wine, brown sugar syrup, etc. Beer can thus be deprived of its bitter taste and potato alcohol of its fusel oil, while putrid water thus loses its foul ingredients.

This filtration through carbon is not to be looked upon as an entirely indifferent process, not only does it alter the concentration of the solutions, but it gives rise to chemical alterations. Various basic metallic salts are thus decomposed, the oxides being deposited. Charcoal withdraws the iodine from a solution of potassium iodide.

The following salts are thus decomposed, so that free acids occur in the filtered solution. Many salts of the fatty acids, morphia acetate and caffeine citrate. Of the inorganic salts, the sodium borate, the alkaline phosphate and metallic sulphates. The following salts are retained in the charcoal entire, undergoing only partial decomposition : many salts of the aromatic acids, such as the sodium carbolate, benzoate and salycilate, so that in this manner the disinfectant power of carbon can be increased, and perhaps practically utilized (Liebermann).

Internally administered the carbon passes off for the most part with the fæces ; but since the very smallest particles are often pointed and have very sharp edges, they can bore their way into the intestinal mucous membrane, and remaining in the tissues, can thus give rise to abdominal pain and diarrhœa. It has been positively shown that carbon, when inhaled, enters into the lungs, the connective tissue cells and lymphatic channels, and thus gives rise to a disease of the lungs (anthracosis pulmonum).

Since carbon everywhere in the organism becomes immediately saturated with moisture, its absorptive power for gas is, for the above reasons, destroyed.

Animal carbon.—On account of the manner in which this form of charcoal is prepared, it presents a much greater superficies than an equal amount of vegetable charcoal, for this reason, and perhaps also on account of the large percentage of salts which it contains, its capability of abstracting materials held in solution is greater than that of wood carbon. It is therefore used by preference for decolorizing sugar solutions.

Therapeutic Application.—Carbon is almost entirely unused by medical practitioners of to-day, and properly so. We need not repeat that its power of absorbing gases can not be utilized internally in such conditions as meteorism. Even if it could exert this power in the intestine, its use might be inadvisable, on account of danger of further irritating the already inflamed intestinal mucous membrane by the sharp particles of carbon. Its former application in purulent surfaces of wounds and ulcers is rendered valueless by the antiseptic treatment of to-day. At the present time it is at most used as a component of tooth powders.

Carbo pulveratus.—Internally it was given in from 0.5–2.0 pro dosi in powders rubbed up with moist sugar preparations ; it is entirely valueless. *Externally* as a dressing it is best used pure.

CARBONIC OXIDE—CARBONICUM OXIDATUM.

When carbonic oxide gas, CO, is inhaled, it abstracts the oxygen from the hæmoglobin and replaces it by carbonic oxide, the result of which is death, with the usual symptoms of asphyxia; this happens also when an indifferent gas, such as hydrogen, is inhaled, the mere want of oxygen causing the asphyxia. Blood and hæmoglobin containing carbonic oxide have a cherry-red color, which persists even after death, because reduction is an impossibility. Carbonic oxide exerts no effect upon any other portion of the body.

Therapeutically the gas is not used.

HYDROGEN—HYDROGENIUM.

Hydrogen, H, is the lightest gas known, colorless and odorless, easily inflammable and entirely indifferent in the animal organism, so that what was said under the head of nitrogen can be affirmed of hydrogen.

HYDROGEN PEROXIDE—HYDROGENIUM PEROXIDATUM.

Hydrogen peroxide, H_2O_2, occurs in large quantities when peroxide of barium, potassium, etc., are decomposed with dilute acids. It is a thick, odorless, colorless and bitter fluid, which is readily decomposed into water and oxygen.

Physiological Action.—Hydrogen peroxide diffuses very rapidly and easily through animal membranes without undergoing any noteworthy decomposition (A. Schmidt).

Assmuth and A. Schmidt injected this material directly into the blood and obtained the following results. If 40 ccm. of the solution, from which 10 times its volume of oxygen may be developed, be injected into the stomach of rabbits, no especial disturbances are observed, although it is absorbed and appears as such in the urine.

If injected into the veins of a dog, in such a manner that it only comes in contact with the blood, 23 ccm. of a solution, which gives rise to 5 times its volume of oxygen, might be injected without danger; vomiting, it is true, rapidly set in, the animal could not stand, and the respiration was slow and difficult, but these disturbances soon passed away. According to this, then, this material is not decomposed in the circulating blood (although this is denied by Guttmann) but if brought in contact with a drop of blood outside of the body it is decomposed with great force. The reasons for this remarkable fact we shall discuss when we come to consider the subject of oxygen.*

When injected hypodermically in rabbits, we have dyspnœa, clonic convulsions, exophthalmos, with dilatation of the pupils and death from asphyxia. After death it was found that the place of injection, as well as the veins and the right heart, were filled with numberless gas bubbles, so that death was caused by the obstruction of the pulmonary circulation with gas bubbles (Guttmann). Both when injected into the stomach or directly into the blood there was a slight increase in temperature up to 0.8°. Whether the amount of carbonic acid excreted was similarly increased was not determined.

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* Compare page 314.

Thenard and Schoenbein showed that not only freshly drawn blood, but a great number of other substances such as seeds, fresh roots of all plants, ferments, especially ordinary yeast, can decompose H_2O_2 by catalytic action, a great deal of gas being given off. So also pus and other exudations from the animal body have the same power. The secretions of chancres and buboes lose their infecting power in the presence of H_2O_2 in somewhat large quantities.

Therapeutically hydrogen peroxide has been very little used. We can therefore express no opinion concerning its utility as a remedy.

OXYGEN—OXYGENIUM.

Oxygen is a colorless, odorless and tasteless gas, non-inflammable, and non-condensible (to a fluid).

It can combine with all the other elements with the exception of fluorine, and it oxidizes all of those. Rapid oxidation gives rise to the phenomena of heat and light, that is to say, combustion takes place.

Oxygen is a component of the atmosphere in which it is mixed with other gases (nitrogen and carbonic acid) and vapor of water; its proportion in the atmosphere is $\frac{1}{5}$ or 21% by volume. In combination with other elements it forms $\frac{1}{2}$ of the crust of the earth, and $\frac{8}{9}$ of the water of the earth.

A modification of oxygen is ozone, or active oxygen, as it is called. Ozone is formed by passing electric sparks through oxygen, or when lightning passes through the air, or where water is decomposed by electrolysis, also when a slow process of oxidation takes place (phosphorus in moist air) or when large quantities of water are rapidly evaporated (at sea and in distilleries). The formation of ozone can be recognized by its peculiar odor and by the turning blue of starch upon the addition of potassium iodide (in the presence of ozone). Since any volume of ozone is less than that of the oxygen from which it was formed, we may look upon ozone as concentrated oxygen. 3 volumes of oxygen are condensed to only 2 volumes of ozone. and since the molecular weight of ordinary oxygen is 32, and that of ozone, 48, a molecule of the former must contain two oxygen atoms, that of the latter 3. Ozone may be reconverted to oxygen by being heated or passed through hot tubes.

Ozone combines more easily and at lower temperatures with the other elements than does oxygen (since one atom is separated and used for oxidation purposes). Ozone can therefore oxidize many bodies at ordinary temperatures, with which oxygen could only combine under the influence of heat.

Physiological Relations.—It is well known that oxygen is absorbed by the higher animals through the lungs, from which it passes into the blood. An adult man requires in 24 hours 520,600 ccm., equal to 946.0 grms. of oxygen. In arterial blood there are on an average 16.9 vol. proc., in venous, 6.0 vol. proc. of oxygen.

The entrance of oxygen into the blood is, to a slight extent, accomplished by simple absorption; to a greater extent by chemical combination. The law of the absorption of gases by fluids, according to which (Dalton-Bunsen) the weight of the amount of gas absorbed by fluids is proportional to the *pressure* under which the gas is placed, does not hold good in this case. Indeed, L. Meyer found that the quantity of oxygen absorbed by the blood, *even under great* pressure, is almost the same as when the pressure is very *slight.* 1 volume of blood which was free from oxygen absorbed, at a temperature of 21°C. about 0.092–0.095 volumes of pure oxygen, although the

pressure varied between 6.8 and 0.5 M. A further proof of the fact is the observation of W. Muller, that the oxygen contained in an inclosed box of air, which was inspired by an animal, is soon entirely absorbed, although the pressure diminishes constantly, with the diminution of the oxygen.

Since blood serum which is free from blood corpuscles absorbs but very little oxygen, 5 times less than blood, under ordinary pressure (Fernet), and never more than ordinary water, it is clear that it is the blood corpuscles which combine with the oxygen. Hoppe-Seyler, indeed, has shown that the hæmoglobin of the blood corpuscles is the substance which combines with the oxygen, even outside of the body, in a crystallized condition (oxyhæmoglobin). Preyer has found that the latter combines with almost as much oxygen, as an amount of blood containing an equal quantity of hæmoglobin. Dybkowsky further found that almost all of the oxygen of the blood is found in the oxyhæmoglobin. 1 grm. of hæmoglobin, at a temperature of 0° and a pressure of 1 M. combines with 1.16 ccm. of oxygen (Hufner).

Although the combination of oxygen with hæmoglobin must be considered a chemical one, it is rather a loose combination, since, under the air pump, or by heating, or by the displacing power of other gases such as carbonic oxide gas, all the oxygen can be withdrawn from the blood. Reducing agents, such as suboxide solutions, ammonium sulphide, sulphuretted hydrogen, also withdraw the oxygen from the blood. On the other hand, the addition of an acid causes a firmer combination with one of the decomposition products of hæmoglobin which the acid has decomposed ; this latter combination is so firm, that it can no longer be pumped out.

For physical reasons the oxygen can not pass directly into the blood corpuscles from the alveoli of the lungs, but even in the minutest capillaries it must first pass through the blood serum. So that the serum must be the first to absorb the oxygen. The inapplicability of Dalton's law (above referred to) to the absorption of oxygen, although the serum does obey this law of the absorption of gases, is explained by the fact that the blood corpuscles always withdraw the oxygen from the serum and bind it (the oxygen) by chemical combination, while the serum is again left free to absorb new portions of the gas from the lungs even at a low pressure.

The reason why the blood can become saturated with oxygen, even when the gas is subjected to so low a pressure as it is in the atmosphere of the lungs, is that the oxygen in the venous blood of the lungs is under a very slight pressure, pressure of (0.760 M–) 00.27 meter (Pfluger and Wolfberg), on account of the chemical combination under which it exists ; this pressure is lower in an atmosphere which contains but a small percentage of oxygen. In other words, no matter how low an atmospheric pressure there may be externally, the pressure of the oxygen in the blood is lower still, so that the direction of the diffusion stream is always from air in the alveoli toward the capillaries.

Behavior of the Organism with the Oxygen in the Atmosphere under Various Degrees of Pressure.—Now we can understand how it is possible for human beings to live under the most variable circumstances, both under very high and very low atmospheric pressure without suffering any sensible disturbance; for the amount of oxygen absorbed by the blood does not depend on the pressure under which the oxygen exists in the blood, but upon the quantity of hæmoglobin in the blood. Arterial blood is always almost saturated (over $^9/_{10}$) with oxygen. The quantity of oxygen contained in the blood of different individuals is various, but only because the amount of hæmoglobin in the blood varies. The amount of oxygen is proportionate to the amount

of hæmoglobin. The animal organism therefore takes up as much oxygen from the highest mountains as from the deepest vales, provided that the amount of hæmoglobin has remained the same, and the quantity of oxygen used up in the tissues has not varied (compare with what is said further on).

It necessarily follows from these observations that neither by the inhalation of pure oxygen nor by increasing the pressure of the inspired air by means of pneumatic apparatus, nor by increased frequency of respiration, are we enabled sensibly to increase the oxygen in the blood, except in so far that the blood serum will absorb a little more oxygen when the pressure is increased, in accordance with Dalton's law, and this increase is so small that we feel warranted in overlooking it. Even in an atmosphere of pure oxygen, warm-blooded animals do not absorb more oxygen or expire more carbonic acid than in ordinary air (Regnault and Reiset); nor were the processes of life carried on any more energetically. Bert has shown that even in an atmosphere of compressed oxygen only a slight increase in the amount of oxygen contained in the blood takes place. So also Buchheim—Hering and Pfluger—Ewald have shown that in the so-called Rosenthal's apnœa the blood shows no or very little increase in the percentage of oxygen (0.1–0 9 vol. proc.) Buchheim therefore very properly observes that suspension of the necessity for respiration can only be due to a diminution in the amount of carbonic acid, or to any alteration in the activity of the respiratory muscles, which results from long-continued artificial respiration. Nobody can suppose that the blood is able to excite normal respiratory movements when the percentage of oxygen which it contains is 17.3 vol. proc., and that it loses this property entirely when the oxygen is present in 17.4 vol. proc.

The contradictory assertions of other experimenters are superficial, subjective and vacillating; they assert, for instance, that the inhalation of pure oxygen is followed by an agreeable sensation of freedom and physical well-being, or, on the other hand, by a painful sensation of burning in the throat and in the breast. Physical power of endurance is heightened, the respiration is lighter and freer, the heart is said to beat more rapidly or slowly. The appetite is improved, symptoms of intoxication are said to take place, there are various sensations in the different nerve tracts; there is a tendency to inflammations, to hæmorrhages; asphyxia can be endured for a longer time. When compared with the above accurate experiments, the material we have just stated is certainly insufficient for the founding of any therapeutic indications for the inhalation of oxygen and the constant recommendations of the latter class of observers for the use of oxygen must be without weight. We do not by this mean to deny the utility of compressed air, but the good results of pneumatic apparatus must be accounted for on the ground that they remove the pathologico-mechanical obstructions and not upon other causes.

The Effect of too High or too Low an Atmospheric Pressure in the Inspired Air.—From what has been said it will be seen that men and animals are independent of the great variations in atmospheric pressure which occur in the normal conditions of life. There is, however, both an upper and lower limit, above which and below which animal life no longer remains unaffected. When the atmospheric pressure of the oxygen is diminished by artificial means, below 0.03 M, or when by ascending in a balloon a point is reached at which the pressure of the atmosphere has fallen below this figure, then the demands of the animal body for oxygen are no longer satisfied, the blood no longer receives the amount of oxygen necessary to life and the organism dies. (W. Muller, Regnault, and Pfluger-Dohmen). The aeronauts Sivel and Croce-Spinelli perished at an altitude of 8,600 M

Their death was probably due, however, not to the low atmospheric pressure (0.262 M. barometer, equal to a pressure of oxygen amounting to 7.0% of one atmosphere), but because in addition to the diminished tension of the oxygen of the air which they inspired, they also made violent muscular exertions; their fellow traveler Tissandier, who remained quiet, lost consciousness but saved his life. Many physiological experiments have shown that death does not set in until the pressure of the oxygen in the inspired air has fallen to 3.5% of one atmosphere.

The symptoms resulting from a deficiency in oxygen are in part those produced by carbonic acid poisoning; dyspnœa, increased blood pressure and diminution in the amount of oxygen absorbed; symptoms of irritation which set in shortly before death are characteristic of deficient supply of oxygen. The symptoms characterizing acute as well as gradual suffocation are due to the deficient supply of oxygen (Friedlander and Herter).

Bert found that the upper limit of the percentage of oxygen that could be endured in the blood of animals was 28–30 vol. proc. (0.76 M. pressure) of their arterial blood; at this point the animals were seized with convulsions, and death set in when this is increased to 3.5 vol. proc. This slight increase in the percentage of oxygen beyond the normal produces an immense increase in the tension of the oxygen of the blood; that of the normal arterial blood is to the fatal tension in blood saturated with oxygen at a pressure of three atmospheres, as 35 is to 2280. According to Bert, death thus produced is due, not to the development of poisonous material under the influence of the high oxygen tension, but because the oxidation process, the consumption of oxygen, and the formation of carbonic acid and urea diminish the temperature; even muscles cut out from the body absorb less oxygen from compressed air, while decomposition as well as fermentation is rendered slower or even suspended under the influence of compressed air. Pfluger calls attention to the fact that this can be compared to analogies present outside of the body, as for example the fact that active phosphorus shines in diluted oxygen but not in pure oxygen.

Is the Oxygen of the Blood in a Neutral or an Active State.—The fact that the oxidations of the body continue even in low temperatures, which is impossible outside of the organism, could be explained it was believed only by the assumption that oxygen was carried in a nascent state (as in platinum black) by the blood corpuscles, as ozone carriers, to the tissues, and that as ozone it there destroys the albumen, the fats and the carbo-hydrates. The observation that outside of the organism, the last named organic compounds can be oxidized by ozone in a similar manner at low temperatures was also in favor of this view. Furthermore, it was believed that the oxygen in the blood gave the reactions of ozone, and hence must be of an ozone nature.

Both Hoppe-Seyler and Pfluger contend against this view from critical and experimental data. According to the latter of these observers, animal oxidation may be compared to the oxidation of active phosphorus in diluted oxygen, where the cause of the chemical combination lies in the phosphorus itself. The oxidation of the animal cell is, within proper limits, entirely independent of the local pressure of the neutral oxygen, and does not necessitate the pressure of active oxygen. All the facts seem to point to the view that the oxygen of the blood is neutral, so that it may have the power of being transported in all directions by the blood corpuscles at the ordinary temperature of the body, as the experiments of Donders have shown. If the oxygen in the blood were converted into ozone it would not possess the necessary mobility which would enable it to undergo diffusion. It could then not come in contact with the tissues.

Pfluger does not consider the Guiac test of A. Schmidt (turning Guiac paper blue with blood) a proof that hæmoglobin is capable of ozonizing neutral oxygen, but accounts for the turning blue of the Guiac paper by the supposition that the coloring matter of the blood is decomposed, and gives rise to the formation of a substance. Hæmochromogen (Hoppe), which has a great affinity for oxygen. But a molecule, which undergoes oxidation at the expense of the atmospheric air, decomposes the molecule of the latter, and thus the ozone which turns blue the Guiac paper is the result of the oxidation of the hæmochromogen. In a similar manner Schmidt's experiments of turning potassium iodide and starch solutions blue, by contact with blood, and decolorizing indigo solutions in the same way, may be accounted for. In both cases there is a series of decompositions combined with oxidations, and the ozone formed as a result of these changes is the active agent, and not the oxyhæmoglobin.

Furthermore, Pfluger brings as a proof for his assertion, the fact that apart from a few very slight exceptions all easily oxidizable substances, which when allowed to stand in the air in alkaline solutions, are not burned up, remain unchanged also in the blood, such are the sodium lactate and grape sugar.

A. Schmidt has noticed the remarkable fact that fresh blood catalyses with uncommon energy hydrogen peroxide; when a drop of blood is added to an almost saturated solution of hydrogen peroxide decomposition immediately results with a violent, explosive ebullition, neutral oxygen being set free, while the hæmoglobin remains unoxidized. Against this fact, which A. Schmidt makes use of to establish this theory of blood ozone, Pfluger cites the experiments first proposed by A. Schmidt himself, and carried out by Assmuth, in which hydrogen peroxide was injected into the blood of living animals without any violent decomposition taking place or the animal suffering the least harm, even when the quantity of hydrogen peroxide was sufficient to have given rise to the formation of 115 cm. of oxygen. From this experiment, Pfluger concludes that the living blood exerts no stronger catalytic action upon hydrogen peroxide than many other substances, but that as soon as it is out of the bloodvessels a product of decomposition appears, which exerts a very powerful catalytic effect upon hydrogen peroxide. So that it is not the ozone of the blood but this unknown product of decomposition which is the cause of this catalytic action.

Finally, in proof of his assertions, Pfluger cites another series of facts, which A. Schmidt himself partly discovered, namely, that serum and blood very rapidly deprive ozonized air of its ozone; and that the oxygen given off from blood under the air-pump does not give the reactions of ozone, although this is the oxygen which has been in combination with the ozone; furthermore, that when ozonized air is passed through the blood or solutions of globuline, the ozone is entirely absorbed by the blood, so that the gas bubbles coming out of the solution no longer give the reactions of ozone, since the ozone has been fixed and utilized for oxidation of the components of the blood; and lastly, that the blood is changed and decomposed by ozone thus passed into it, the albuminous components becoming oxidized, the blood corpuscles dissolved, and even the coloring matters gradually destroyed. It appears, therefore, in fact, that the theory that oxygen is converted into ozone by the hæmoglobin is untenable. In consideration then of the real relationship of the oxygen to the blood, the theory of the physiological oxidation in the living body will have to be modified to the effect *that oxygen is bound by the hæmoglobin* of the blood in an entirely

neutral condition, and that it does not enter into an active state anywhere in the circulation.

As to whether oxygen is ozonized in the tissues, Pfluger considers it not entirely impossible, but as yet unproved.

What is the part taken by Oxygen in the Organism?—The living blood itself is not indifferent to oxygen, and possesses a sort of respiration of its own; that is to say oxidation processes are continually taking place in the blood, as will be seen from the following series of experiments: 1. Living arterial blood, kept at the ordinary temperature of the body, darkens (that is approaches the venous condition) not only in the living artery, but even in glass vessels from which the air has been entirely excluded. Since in the latter case it does not come in contact with any other animal tissue, it follows that the free oxygen of this blood must have been put in firmer combinations in the blood itself; if blood fresh from the artery be allowed to cool immediately to 0° C., it remains of a bright red color, because the cold prevents or retards the oxidation processes (Pfluger.) 2. If oxygen be withdrawn from the blood by means of the mercury pump, we obtain a greater quantity of the gas if the exhausting process be carried on very rapidly. By the aid of Pfluger's exhausting method, which takes from one to two minutes, the average amount of oxygen which can be obtained from certain specimens of blood is 16.9% (at 0° C. and 1 M. of Hg pressure), while if the exhausting process take a longer time only 15.3% can be obtained from similar specimens of blood (at 0° C. and 1 M. of Hg pressure). 3. A. Schmidt has shown that easily oxidizable substances (the so-called reducing bodies, which originate from the tissues) occur in venous blood (blood of the asphyxial condition) in large quantities. If such blood, containing only a trace of oxygen, be shaken up artificially with oxygen, the oxygen is absorbed very rapidly, while CO_2 is only gradually formed. Arterial blood shows this only to a slight degree, so that we are warranted in the conclusion that in venous blood more reducing materials are present than in arterial; for in the latter these substances have been rapidly oxidized by the oxygen which it has absorbed.

But the oxidation processes taking place in the living blood itself are very slight, as was very clearly shown by Pfluger, in opposition to Estor and St. Pierre and Hoppe-Seyler. A comparison between the color of the blood in the arteries nearest and furthest from the heart, as well as the most accurate differential gasometric analyses shows that as long as the blood circulates in the arteries there is no noteworthy variation in the percentage of oxygen which it contains.

Tissue Respiration.—In the capillary circulation the largest portion of the oxygen of the blood disappears, and large amounts of carbonic acid begin to appear. The following questions here present themselves: Does the oxidation which leads to the formation of carbonic acid, take place in the blood itself or in the tissues, that is in the cells? 2. Granted that the latter is the case, does oxygen pass directly into the cell, and does CO_2 pass from the latter into the blood, or does the interchange take place in another manner, for instance, by means of peculiar, ferment-like carrying bodies? Pfluger has shown it to be very probable that these processes of oxidation which lead to the disappearance of the oxygen, and the formation of carbonic acid, do not take place in the blood itself, but in the tissues. To show how probable this is Pfluger calls attention to the large quantities of oxygen which are diffused through the walls of the capillaries of the lungs; at least 58 times the quantity that the plasma could contain at any given instant even if it were saturated.

Even the slightest variation, therefore, in the already very low local pressure of the oxygen in the tissues must have an immense influence in accelerating the diffusion stream of oxygen which is directed toward it. The fact that no one has been able to prove the presence of oxygen, as such, in the tissues, shows that the tension of the oxygen in the tissues must be almost at a minimum.

Besides this we must remember how extraordinarily well the organism is fitted for purposes of diffusion ; we should remember over how great a surface the blood is distributed when it circulates in the body in millions (according to Vierordt, 8 millions) of thin threads (capillaries), communicating with the tissues by means of diffusion, its parts being constantly in motion and its superficies being constantly renewed. Again, it is only necessary to remember the very short space over which the diffusion stream has to pass, and the rapidity with which the oxygen combines, in the extra vascular cells, with bodies in which it is not held in a free condition, but in which it loses its tension entirely.

So that, even if the pressure of the oxygen in the blood corpuscles is not high, yet in consideration of the circumstances just mentioned, that in the tissues themselves the local pressure of the oxygen is infinitely lower, even than in the blood corpuscles, the flow of oxygen from the blood into the tissues must be enormous.

That oxidation does take place in the cells is shown also by facts derived from comparative physiology (the respiration of the lowest single cell, that is to say, bloodless organisms, etc.), as well as by observations on the higher animals. Here even after the capillaries have been deprived of all blood, the muscles still possess a weak respiration of their own, and muscular movements, with which oxidation is necessarily connected, are possible with blood free from oxygen. Furthermore, Pfluger and Strassburg, in a work on the topography of the tension of gases in the organism, showed that CO_2 is principally formed in the tissues. Where CO_2 originates, to that place oxygen must pass from the blood.

The only objections against this view would be that reducing substances might possibly diffuse into the blood out of the cells more rapidly than the oxygen diffuses from the blood into the cells and there take up most of the oxygen. Such an objection would be opposed, however, by Pfluger's observation that warm venous blood when saturated with oxygen only binds minimum quantities of oxygen (because the reducing substances are already oxidized) and yet large quantities of oxygen are constantly disappearing from the capillary blood ; in venous blood there should be found, according to this theory, at least as much oxygen as in the capillaries, which is certainly not the case. The amount of carbonic acid given off by warm venous blood when shaken with oxygen was also very small. We can now then add a fact that must be accepted as true, that the giving up of oxygen and the formation of carbonic acid are two processes which take place together, but do not depend directly one upon the other.

In what manner and by what means is the amount of the oxygen absorbed, regulated ? The amount of oxygen absorbed into the organism depends entirely upon the amount that is used up. For since the blood corpuscles in the pulmonary vessels attain almost an invariable point of saturation with *oxygen,* they absorb necessarily in the pulmonary circulation more oxygen *the poorer they* have become in oxygen while passing through the systemic *circulation,* because of the oxidation processes taking place in the body. But *the oxidation processes* in the body are increased, for example, by muscular *labor, during* the process of digestion, or when the body is surrounded by a

lower temperature ; and diminished when the blood is poor in consequence of hæmorrhages, etc. Lothar Meyer therefore concluded that the hæmoglobin was the regulator of the amount of oxygen used up iu the body. But this view can not be maintained, for it cannot be doubted that the organism absorbs more or less oxygen according to the amount of work performed, food taken, etc., without any alteration in the amount of hæmoglobin in the blood taking place. Besides this, Tinkler has shown that even a great loss of blood does not, even after the lapse of a very short space of time, show any sign of exerting any influence upon the amount of oxygen which is used ; again, the amount of oxygen used in the body is entirely independent of the rapidity of the circulation of the blood.

Pfluger supposes that the animal cell itself regulates the quantity of oxygen brought to the tissues in consequence of the extraordinarily low attraction power which is necessary for the diffusion of the oxygen. As soon as the tissue needs more oxygen on account of an increase in the activity of the processes of life, the local pressure of the oxygen in that tissue is slightly diminished (perhaps to an extent unappreciable by our methods) and the diffusion stream is correspondingly increased. Here alone lies the secret of the method by which the amount of oxygen supplied to the system is regulated ; the cell itself determines it, not the amount of oxygen contained in the blood, or the tension of the aortic system, or the rapidity of the circulation of the blood, or the "modus of respiration." All of these elements are secondary and subordinate. They combine in their action to subserve the purposes of the cells, which do the real work of the organism, and which are among themselves arranged in a proper series of subordination one to another, so that a superior class consisting of a few cells, namely, the nerve cells, governs the intensity of the living processes taking place in almost all the other cells, in accordance with a feeling of well being, which is produced by the normal temperature relations of the blood.

How can the oxidation processes of the living body, however, be explained without supposing that active oxygen is the cause of these oxidations ? Pfluger's idea that these processes take place under the influence of neutral oxygen is again opposed by the same objection which we mentioned when discussing the question whether oxygen is present in the blood in the form of ozone, namely, that most of the materials of our food and those present in the blood (especially the albuminoid bodies) are entirely unaffected by neutral oxygen at the ordinary temperature of the body. Pfluger solves this objection by the following considerations, which we give as completely as possible :

He concludes that not the oxygen but the albumen is changed, when, after being taken up into the living cell, it has become an integral portion of the the organism. "An albuminous molecule, which in the gray cortex of the brain, assists in the formation of thought, in the spinal cord, transmits sensation, in the brain, various mental energies in the muscle performs mechanical labor, in the glandular cell aids in excretion and secretion, originated from the same albumen, but has been converted into something else in the cells. That the albumen of the testicle is converted into spermatozoa, that of the brain into 'thought substance,' that of the muscle into contractile material depends upon the cell which absorbed the nutritive albumen ; as soon as this absorption has taken place, it loses its indifference to neutral oxygen, that is to say, it begins to breathe and to live. For all of the specific activities of life, procreation, assimilation, growth, increase, sensation, thought, will, motion, etc., is the work of the cell substance and not of the fluids. The cell alone gives specific signs of life, and it alone is alive in the true sense of the

word. The albumen of the blood plasma is dead in the living body as long as it has not been converted into cellular substances."

One of the greatest points of difference, however, between albumen which has been converted into cell substances and simple nutritive albumen, is the surprising readiness with which the former undergoes decomposition, the influence of ferments being entirely unnecessary. Living material is not only readily decomposed, but is to be considered as constantly undergoing decomposition. There is no way in which a portion of living tissue can be kept from undergoing decomposition. Life and decomposition are one. The living decomposibility is the reason of its irritability.

"Are they not indeed infinitely small living forces, upon which a ray of light acts, until they produce the most powerful effects upon the retina and upon the brain? Is not the slightest irritation produced by the point of a needle passed over a naked muscle sufficient immediately to give rise to a contraction with the simultaneous formation of carbonic and lactic acid? and how infinitely small are the living nerve forces, by the aid of which they are able to powerfully increase the processes and chemical actions going on in the organs?" Pfluger accordingly distinguishes between substances which are living and those which are capable of life. A grain of wheat, a bird's egg, are not alive, but by the aid of warmth and moisture capable of becoming alive.

Therefore although substances capable of life can only be oxidized at low temperature by the aid of ozone, it does not follow that really living substances can not, in consequence of their readiness to undergo decomposition and the mobility of the intramolecular structure, be oxidized by ordinary oxygen; indeed, they are as readily thus oxidized as the non-living substances are by ozone.

We are not able to describe in all its details the great function of the oxygen in the animal organism. Animal life, indeed, depends chiefly upon the entrance of the greater part of the body into a combination with oxygen. It is a continual process of oxidation and burning, by which the complicated combinations which have been produced by a process of synthesis in the plants, and introduced in the animal body with the food, are decomposed into simpler forms and those richer in oxygen, until finally they have attained those forms which are simplest and richest in oxygen, namely, water, carbonic, phosphoric and sulphuric acids, under which forms they are excreted from the body. Animal life, therefore, depends upon a constant decomposition, or rather renewal, of the portions of the body, and can be compared to a burning flame, which retains its form while its parts are constantly altered and changed by oxidation. Complicated food materials must be introduced and burnt up by the oxygen. Dearth of the latter in warm-blooded animals kills in a few minutes, while want of the former can be endured for weeks. Although Pfluger has shown that in the cold-blooded animals the functions of life can go on, in the ordinary manner, for 24 hours without a trace of oxygen being introduced, this is only due to the slow using up of the intramolecular oxygen in these animals.

Effects of Ozone inhaled or absorbed from without upon the Organism.—After having seen that oxygen inhaled in any manner whatever, has no other effect than the ordinary air of the atmosphere, which contains oxygen, and furthermore, that in certain pathological conditions, we can only aid respiration by alleviating certain mechanical hindrances, and that here even pure oxygen has no other effect than ordinary air, we must study the effect of the inhalation of ozone upon the organism. Here also impartial observation will teach the futility of a great many sanguine hopes. For the only utility of a

large percentage of ozone in atmospheric air would lie in the fact that the ozone, by destroying low forms of organisms and septic elements, would render the air purer, and thus an atmosphere rich in ozone as that on the ocean or sea, might be healthier than air as ordinarily found over the land. On the other hand ozone, whether inhaled or internally administered (ozone water) can not reach the blood as such, because it finds enough upon the mucous membranes of the body with which it combines, and thus loses its active character. Upon dry mucous membranes, those free from mucus, it may produce an inflammation on account of its strong affinity, thus giving rise to catarrh of the nose, larynx and bronchi, and thus causing disease. Small animals (mice and rabbits) indeed die when the quantity of ozone in the air is 1 to 6000 or even 1 to 2000 (Schoenbein). Death is preceded by severe irritation and disturbance of the respiration with symptoms of collapse; while even men show irritative symptoms after breathing too large quantities. But even if ozone reached the blood as such, which is impossible, it would have a destructive action upon the components of the blood and thus again exert an injurious effect.

The proof which we have given that ozone is entirely unnecessary to the processes of life destroys the whole theory of the ozone treatment of disease.

Therapeutic Application.—As soon as oxygen was discovered, the most extravagant things were expected from its therapeutic application. From what has been said, it will appear that even theoretically the progress of physiological science has shown these hopes to be groundless, for the organism does not take up more oxygen from an atmosphere very rich in oxygen than it does from ordinary atmospheric air. Good pure air, free from injurious gaseous or solid impurities, therefore, has the same therapeutic effects as the inhalation of pure oxygen.

This *a priori* conclusion, based upon theoretical knowledge, is fully confirmed by impartial observation. Oxygen was recommended immediately after its discovery in the most various pathological conditions. The first enthusiasm, however, was followed by an entire change of opinion, and it is not until recent years that oxygen was again recommended by some physicians. But even this recent experience confirms our opinion that oxygen has very little value if any as a therapeutic agent. We therefore think it unnecessary to discuss all of the uses for which it has been recommended, and shall refer, for the sake of completeness only, to those conditions in which there has been a more general experience of its application.

Naturally, the gas was first tried in diseases of the respiratory organs. Experience has shown that oxygen inhalations should be avoided in all acute inflammatory processes of these organs. In phthisis, in which at first great results were expected from its use, it has generally shown itself useless, sometimes even injurious, because it increased the fever, and even hæmoptysis was thus produced. Some favorable results have, it is true, been reported, but these are so few that, in our opinion, they need further confirmation. If the inhalations are used at all, it should be in cases in which there is no tendency to hæmorrhages. Lyden and Jaffe recently obtained favorable results from oxygen inhalations in diseases of the lungs, of which a putrid process is a part of the pathological condition—such as bronchitis putrida and gangrene of the lungs. The odor and amount of the eruption were diminished, and the general condition of the patient was improved.

Oxygen has most frequently been used in conditions of dyspnœa, and where the circulation was overloaded with carbonic acid. First of all in asthma, it appears, most of these cases were chronic catarrh with acute exacerbations accompanied by cyanosis and dyspnœa. In many cases the

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